Endovascular treatment in elective and ruptured abdominal aortic aneurysms

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Arnoud Gerardus Peppelenbosch

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Promotor:

Prof.dr. M.J.H.M. Jacobs

Copromotores:

Dr. J. Buth (Catharina Ziekenhuis, Eindhoven)
Dr. G.W.H. Schurink

Beoordelingscommissie:

Prof. Dr. P.J.E.H.M. Kitslaar (voorzitter)
Dr. R. Balm (AMC, Amsterdam)
Prof. dr. J.D. Blankensteijn (UMC, Nijmegen)
Prof. dr. J.M.A. van Engelshoven
Prof. dr. J.G. Maessen

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CHAPTER I

General Introduction

Abdominal aortic aneurysms

An aneurysm is defined as a "permanent, localized dilatation of an artery having at least a 50% increase in diameter compared to the expected normal diameter of the artery in question".[1] Although aneurysms can be present at every site of the aorta, its predominant site is in the abdominal aorta, which is the localization in over 75%.[2] The overall prevalence of abdominal aortic aneurysms (AAA) in The Netherlands in individuals of 55 years of age or older has been estimated at 2.1%; in males 4.1% and in females 0.7%.[3] This is in concordance with estimates derived from large screening studies from other countries, which indicated a prevalence in males of 65 years of age or older between 4.3% and 8.8%. Risk factors for AAA included advanced age, male gender, smoking, positive family history for AAA, atherosclerosis and hypertension.[4,5]

Risk factors for rupture

An abdominal aortic aneurysm does not cause any complaints until rupture occurs (rAAA). Typically a rupture presents with acute abdominal pain with or without back pain and is often combined with signs of haemodynamic shock. At physical examination a pulsatile mass in the abdomen is present in more than half of the patients.[6] The relationship of aneurysm size and the incidence of rupture was assessed in a number of reports. The best treatment of small aneurysms, i.e. with a diameter of 4.0 to 5.4 cm, was assessed in two randomized trials by comparing immediate repair with continued surveillance of AAA. An annual rupture rate of 0.6 to 1% was observed in these small aneurysms without intervention.[7,8] In contrast, in larger aneurysms, with a diameter of 5.5 to 6.0 cm, a one-year incidence of rupture of 9.4% was observed. This assessment was performed in patients who were unfit for AAA treatment or refusing the procedure.[9] Brown and colleagues demonstrated also in patients considered unfit for operation an annual rupture rate of 15.6% in men and 30.5% in women with AAA diameters of 6.0 cm or greater.[10] Although the latter reports represented a selected patient group these studies suggested that the risk of rupture was dependent on size of the aneurysm. Other risk factors for rupture included female gender, smoking and positive family history for AAA.[7,10,11]

Indications for treatment

When no treatment is performed for a ruptured AAA, the median survival time from arrival at the hospital until death has been estimated in a number of studies between 7 and 10 hours.[12,13] The maximum survival time in these studies, without intervention was 6 days. Rupture of an AAA is always lethal unless an intervention is performed with exclusion of the ruptured aneurysm from the systemic circulation either by open or by endovascular technique. Because the outcome of treatment of ruptured AAA is associated with a very high morbidity and mortality current clinical strategies aim to prevent rupture. Treatment of an a-symptomatic aortic aneurysm is indicated when

the risk of rupture outweighs the risk of operation. Consequently the decision for an elective repair depends largely on the risk of the procedure. In published series the 30-day or in-hospital mortality of elective open repair ranged from 3.8% to 8.2%. This rate needs to be compared with an annual rupture rate of untreated aneurysms with a diameter between 5.5 - 6.0 cm of 9.4%.[9] Currently 5.5 cm is generally accepted as the cutoff point for elective open repair. The diameter threshold for an indication of repair in women is probably lower, although no accurate criteria have been established for females. However, one must consider the patients' condition and his or her life expectancy. In the case of a poor risk patient one may want to choose a higher threshold diameter. The aneurysm diameter is important not only to determine the risk of rupture and confirm the indication of an intervention. As we have observed the pre-operative diameter of the aneurysm also appears a parameter for early and late mortality after treatment of the aneurysm. This aspect has received little attention previously. In *Chapter II* a correlation is described between aneurysm size and outcome after endovascular repair.

In case of rupture of an abdominal aortic aneurysm the only possibility for surviving is exclusion of the ruptured aneurysm from the systemic circulation. This treatment was first reported by Gerbode in 1954, who resected an aneurysm and replaced it with an aortic homograft.[14] At the current time prosthetic materials have replaced homografts and operative techniques have been modified by an inlay technique. The procedure is finalised by closure of the aneurysm wall instead of resecting the aneurysm. However, the main principles of the operation as performed by Gerbode have remained unchanged. Most frequently a midline laparotomy is performed. The proximal aorta is dissected free to enable crossclamping. This manoeuvre is the first step of the operation and will allow quick control when sudden bloodloss occurs during further dissection of the aneurysm. After crossclamping, the aneurysm is opened and backbleeding from lumbar arteries is controlled by suture-ligation. Then a prosthetic tube or a bifurcation graft is inserted by proximal and distal anastomoses. By releasing the aortic clamp the bloodflow to the lower legs is reestablished. Finally the aneurysm wall and the posterior peritoneum is closed to cover the prosthesis. The reported outcome of this operation for ruptured AAA involved a 30-day or in-hospital mortality ranging between 32-70%.[6,15-20] A recent meta-analysis estimated a one-month mortality rate in the year 2000 of 41%, based on a decline in the mortality of 3.5% per decade.[21]

In 2000 the total number of patients admitted because of a rAAA to hospitals in The Netherlands was 916, of whom 653 (71.3%) died. This death rate regarded also patients presenting to the hospital who were not offered treatment for various reasons.[22] When the overall community death rate was regarded this was even higher with mortality rates of 79-88%, including patients with advanced age and those who did not reach the hospital alive.[23,24] The reported incidence of patients with rAAA reaching the hospital alive varied between 6-12/100.000.[12,19,25] The incidence of rAAA in the Swedish population was estimated by Johansson and Swedenborg at 29-38/100.000.[26] Rupture of the untreated aneurysm is always fatal. However, even after

a successful operation the outcome is uncertain and the recovery often cumbersome. The poor short-term survival of rAAA contrasts with the long-term results in survivors. In terms of quality-of-life the outcome in survivors is almost similar compared to the general population.[27,28]

Endovascular treatment

Endovascular treatment of elective abdominal aortic aneurysms was introduced by Parodi and colleagues in 1991.[29] They reported their experience in 5 patients with AAA who were unfit for open repair. Patients were treated, using local or regional anaesthesia, with a balloon-expandable stent attached to a polyester tubular prosthesis. Retrograde cannulation of the common femoral artery was used to insert the stentgraft. Although Parodi was the first to publish the first successful experience with stentgraft treatment of aneurysms in the English literature a few years earlier a Russian publication had described the same technique.[30] Since these first publications endovascular abdominal aortic aneurysm repair (EVAR) has gained an increasingly important role in the clinical management of abdominal aortic aneurysms. Reports on elective AAA repair with EVAR have shown promising results and several advantages of this minimal invasive technique were observed including reduced cardiac stress during the procedure and reduced mortality post-operatively.[6,7,31] The use of emergency EVAR for rAAA was a natural development. The first report came from Yusuf and colleagues in 1994. They treated a 61 year old male patient with a 6 cm rAAA with an aorto-uni-iliac stentgraft in combination with a femoro-femoral crossover bypass.[32] After this initial experience it took 6 years before the first institutional series was published. Ohki and Veith published in 2000 the first 20 selected patients with rAAA treated with emergency EVAR (eEVAR). The reported mortality rate in this series was 10%.[33] In this thesis one of the early reports on the feasibility of eEVAR is included. In the following section the developing experience with emergency endovascular repair of rAAA in the Catharina hospital in Eindhoven, where this thesis was accomplished, is summarised. Research questions associated with the risk of rupture of intact AAAs evolved during the study period and were addressed in related chapters (*Chapter II*).

Experience with eEVAR in the Catharina hospital and clinical studies used for this thesis

The first patients with a ruptured AAA who underwent endovascular repair were treated in 2000. An initial concern involved training of paramedical staff and the logistics of the "new operation". Patients with a ruptured aneurysm may present at the hospital at any hour of the day or night. As a consequence the procedure often has to be performed with operating room personnel who have little or no practical experience with

endovascular interventions. Therefore it was essential to simplify the stentgraft procedure considerably when it needed to be performed in the emergency situation. The vascular surgical staff fell back on a technique that had been used in the early days of elective EVAR, the aorto-uni-iliac stentgraft with endovascular occlusion of the contralateral iliac artery and a crossover femoro-femoral bypass. This concept was modified to make it suitable for emergency use. Medtronic-AVE was willing to manufacture this adapted system and has marketed it as the "Emergency AAA kit".

Emergency EVAR starts with the exploration of one groin under local anaesthesia. Guidewires and angiography catheters are introduced in the femoral artery with a seven French introducer sheath. Using digital subtraction angiography the renal arteries are located and marked on the fluoroscopy screen. The proximal part of an aorto-uni-iliac TALENT® device is then introduced and deployed with it's upper markers just below the renal arteries. Subsequently the distal part is introduced and deployed. Efforts are made to spare the inflow in the ipsilateral hypogastric artery by choosing the distal landing zone in the common iliac artery. Distal sealing in the external iliac artery should be avoided since this causes overlapping of the hypogastric artery and obstruction of this vessel. This is to reduce the risk of colon ischaemia and other complications. After the distal device is deployed the second part of the operation takes place. The contralateral common femoral artery is explored to introduce the occluder device to block the corresponding common iliac artery and prevent retrograde perfusion and pressurisation of the aneurysm. In case the contralateral common iliac artery is aneurysmatic, the contralateral external iliac and hypogastric artery are both ligated via a small retroperitoneal lower quadrant approach. A femoro-femoral crossover bypass is performed to complete the operation. A completion angiogram is performed to identify endoleaks and to assess whether the device has been correctly placed. Type II endoleaks may be accepted as these often occlude spontaneously in the postoperative period. Type I or III endoleaks have to be dealt with at the initial operation, either by extension cuffs or in the case of a proximal type I endoleak occasionally by the deployment of a balloon expandable bare Palmaz stent to increase the axial force at the most proximal segment of the stentgraft.

Chapter III reports on the treatment of a series of selected patients with eEVAR. During the recent years several publications demonstrated the feasibility of eEVAR in rAAA often with substantially lower 30-day mortality rates than in series of rAAA treated by open repair.[34-38] Mortality rates in these eEVAR-series with selected patients varied from 0 to 45% while several publications reported a mortality of approximately 10%. However, the number of patients reported in these institutional series were small, varying from 4 to 21, which detracts from the validity of the observed low mortality rates. Comparison of the different series was problematic due to varying inclusion criteria. For example, in some articles the reported experience included patients with symptomatic non-ruptured AAA (snrAAA) and patients with rAAA combined. In addition in some series the use of either aorto-uni-iliac or bifurcated devices was reported. In all published series a selection bias was likely. Patients treated with eEVAR were selected on the basis of haemodynamic stability, e.g. absence of shock, and morpho-

logy, e.g. favourable configuration of the neck and iliac arteries. The absence of shock and a favourable morphology most likely caused an advantage in survival in favour of the eEVAR group. Possibly a large majority of these patients would also have survived open repair. In most reported papers it was unclear what the mortality in the overall group of patients with rAAA was, e.g. patients treated with eEVAR and with open repair combined in the same period in the same institution. Thus, the true impact of the use of eEVAR in the entire treated group with rAAA was not assessed in any previous studies.

In the current thesis an institutional patient-cohort constituted according to an intent-to-treat by eEVAR protocol is included. This series consisted of the entire cohort of patients with rAAA, i.e. those treated by open repair and those treated with eEVAR. The advantages of this study design over the earlier reports involved the assessment of the feasibility rate, e.g. in how many rAAA patients can eEVAR be performed? This is an important issue as the advantage of eEVAR would be limited if only a minority of patients with rAAA can be treated by eEVAR. Secondly, the reasons for exclusion from eEVAR and the logistic problems of the implementation of this new technique in an institution were to be assessed. Thirdly, different from previous series, this analysis may provide an insight on the impact of eEVAR on the early mortality in an unselected cohort of patients with rAAA. The outcome of this institutional study is reported in *Chapter IV*.

Several issues such as complications associated with eEVAR had not been assessed previously in the literature, like the risk of branch ischemia affecting the spinal cord. Its incidence in rAAA patients receiving open repair has been reported between 1 and 2.8%.[39-41] Paraplegia following eEVAR had been reported in one single case previously.[42] The incidence, riskfactors and consequence of spinal cord ischaemia after eEVAR were assessed and the outcome is reported in *Chapter V*.

In the analysis described in *Chapter IV*, which regarded the experience of the Catharina Hospital, we had combined patients with snrAAA and with rAAA patients. Patients with rAAA represent the most challenging and better defined category and we directed further clinical studies on these patients. The number of patients with rAAA, treated by eEVAR was small (16 patients). A validation of the results of emergency EVAR in patients with true ruptured AAA required a larger series. Fortunately our department was given the opportunity to organise a multicenter study, which was sponsored and supported by Medtronic AVE. A pragmatic trial needed to be proposed to the sponsor and participating centers. A randomised controlled trial is considered to provide the highest level of scientific evidence about the relative value of a new treatment method. However, a randomised trial of eEVAR in patients with rAAA and a comparison with open repair did not seem practical at the current time. In addition, a randomised trial would have required a very large series to obtain sufficient statistical power, while useful data could be obtained from a smaller non-randomised comprehensive feasibility study including all-comers with rAAA.

A number of other issues were expected to set back the endovascular technique. Firstly, the logistics of the new emergency endovascular procedure needed to be

organised in the participating institutes. Secondly, the extend of the learning process of endovascular specialist teams was not accurately known. Although all teams had documented experience with eEVAR their learning process still could be a disadvantage for the endovascular technique. In this multicenter cohort study an intent-to-treat by eEVAR, or preferential eEVAR, strategy was chosen. The main reasons for exclusion of a patient from eEVAR were severe haemodynamic instability that would not allow CT examination or an angiogram or an unfavourable anatomy that would not allow eEVAR (access iliac arteries or infrarenal neck). The logistic issues were outlined in detail in the study protocol and discussed with staff members in the individual centers. In the protocol the work-up and treatment of the rAAA patient was described from first presentation in the hospital. We included all enrolled rAAA patients regardless whether the procedure was by endovascular technique or open repair in the study group. The outcome in the study group was compared with literature data. The design and protocol of this study is reported in *Chapter VI*.

The outcome of the New ERA trial (Endograft treatment in Ruptured abdominal aortic Aneurysm) is presented in *Chapter VII*. This report described an international multicenter cohort study of patients with rAAA, who were treated preferentially by eEVAR. The outcome in this group was compared with that of patients treated by conventional open surgery as reported in the literature.

Summary of the objectives of this thesis

1. To assess the influence of aneurysm size on the early and late outcome of EVAR.
2. To evaluate the outcome of an institutional series of rAAA patients who were treated preferentially by eEVAR.
3. To assess the incidence and risk factors for spinal cord ischaemia in rAAA patients especially those treated by eEVAR with an aorto-uni-iliac device.
4. To describe the design of the protocol and report the results of an international multicenter cohort study of patients with rAAA, treated preferentially by eEVAR.

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CHAPTER II

Diameter of abdominal aortic aneurysm and outcome of endovascular aneurysm repair: Does size matter? A report from EUROSTAR

N. Peppelenbosch, J. Buth, P.L. Harris, C. van Marrewijk, G. Fransen

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Abstract

Objectives: This study was undertaken to determine the effect of the preoperative diameter of abdominal aortic aneurysmson the midterm outcome after endovascular abdominal aneurysm repair (EVAR).
Method: The data for 4392 patients who had undergone EVAR were analyzed. Patients were enrolled over 6 years to June 2002 in the EUROSTAR database. Outcomes were compared between three groups defined by the preoperative diameter of the aneurysm: group A (n=1962), 4.0 to 5.4 cm; group B (n=1528), 5.5 to 6.4 cm; and group C (n=902), 6.5 cm or larger. Patient characteristics, details of aortoiliac anatomy, operative procedures, old or current device generation, and postoperative complications in the three patient groups were compared. Outcome events included aneurysm-related death, unrelated death, conversion, and post-EVAR rupture of the aneurysm. Life table analysis and log-rank tests were used to compare outcome in the three study groups. Multivariate Cox models were used to determine whether baseline and follow-up variables were independently associated with adverse outcome events.
Results: Patients in group C were significantly older than patients in groups A and B (73 years vs 70 and 72 years, respectively; P=.003 – P<.0001 for different group comparisons), and more frequently were at higher operative risk (American Society of Anesthesiologists classification >3; 63% vs 48% and 54%; P=.0002–P<.0001). Device-related (type I) endoleaks were more frequently observed at early postoperative arteriography in group C compared with groups A and B (9.9% vs 3.7% and 6.8%; P=.01–P<.0001). Postoperatively systemic complications were more frequently present in group C (17.4% vs 12.0% in group A and 12.6% in group B; P<.0001 and .001). The first-month mortality was approximately twice as high in group C compared with the other groups combined (4.1% vs 2.1%; P<.0001). Late rupture was most frequent in group C. Follow-up results at midterm were less favourable in groups C and B compared with group A (freedom from rupture, 90%, 98%, and 98% at 4 years in groups C, B, and A, respectively; P<.0001 for group C vs groups A and B). Aneurysm-related death was highest in group C (88% freedom at 4 years, compared with 95% in group B and 97% in A; P=.001 and P<.0001, respectively; group B vs A, P=.004). The annual rate of aneurysm-related death in group C was 1% in the first 3 years, but accelerated to 8.0% in the fourth year. Incidence of unrelated death also was higher in groups C and B than in group A (76% and 82% freedom at 4 years vs 87%; P<.0001 for both comparisons). Ratio of aneurysm-related to unrelated death was 23%, 21%, and 50% in groups A, B, and C, respectively. Cox models demonstrated that the correlation between large aneurysms (group C) and all assessed outcome events was independent and highly significant. Older generation devices had an independent association with aneurysm-related and unrelated deaths (P=.02 and P=.04, respectively). However, this correlation was less strong than large aneurysm diameter (P=.0001 and P=.0009, respectively).
Conclusions: The midterm outcome of large aneurysms after EVAR was associated with increased rates of aneurysm-related death, unrelated death, and rupture. Reports

of EVAR should stratify their outcomes according to the diameter of the aneurysm. Large aneurysms need a more rigorous post-EVAR surveillance schedule than do smaller aneurysms. In small aneurysms EVAR was associated with excellent outcome. This finding may justify reappraisal of currently accepted management strategies.

Introduction

Endovascular aneurysm repair (EVAR) has gained an increasingly important role in clinical management of abdominal aortic aneurysms since its introduction in the early 1990s. The availability of EVAR may change hitherto accepted surgical decision-making for abdominal aortic aneurysm (AAA) repair. In conventional surgical AAA repair the risks of the procedure are considerable, and must be considered against the benefits of preventing death from rupture. Similarly, differences in early and late outcome after EVAR must be balanced against the natural history of untreated AAA. Since the publication by Szilagyi et al,[1] size of the aneurysm has been recognised as the predominant risk factor for death from rupture, with low risk associated with small aneurysms, intermediate risk with medium-sized aneurysms, and dramatically increased risk with large aneurysms.[1-6] The definition of a small aneurysm has changed somewhat after recently published results of two trials that compared the outcome of an initially conservative approach with primary open repair.[7,8] The threshold diameter for a small aneurysm in both trials was 5.5 cm, as measured on the largest section of the aneurysm. Randomised comparative studies for aneurysms with diameter larger than 5.5 cm are generally considered unethical, on the basis of indirect but compelling evidence of high risk for rupture from natural history studies in patients unfit for open repair or refusing treatment.[5,6,9,10] A large number of cohort studies of open AAA repair, published over two decades, have identified several patient-related variables that determine either excellent or less optimal operative or long-term outcomes of treatment, with age, female gender, comorbid conditions, and required level of aortic clamping the most frequently cited risk factors.[11-13] However, almost all series on open AAA repair have neglected to assess the achieved modification of the risk for rupture according to patient cohorts stratified according to aneurysm size. In contrast, in a previous publication on the EUROSTAR collaborative series on patients unfit for open repair undergoing EVAR, a positive correlation was observed between comorbidity-related and aneurysm-related death, and larger aneurysm size.[14] Mean-while, a few other studies on outcome of EVAR have demonstrated this correlation of aneurysm size with mid-term outcome after treatment as well.[15-17] The objective of the present study was to assess the influence of aneurysm size on the early and late outcome of EVAR in the entire prospectively enrolled series of patients in the EUROSTAR database.

Method

Data for 4392 patients operated on over 6 years, ending in June 2002, who were enrolled prospectively in the EUROSTAR database constituted the basis of this analysis. An account of the organization of the EUROSTAR Registry and reports on various aspects after EVAR have been published.[18-20] For all patients, minimal follow-up was 1 month. Patients with an aneurysm smaller than 4.0 cm in diameter, including those with large iliac aneurysms, had been excluded from the study cohort. This cohort represents patients from 110 European institutions. All patients received commercially available, CE-approved devices, including AneuRx, EVT/Ancure, Excluder, Stentor, Talent, Vanguard, Zenith, and "other." Four thousand fifty (92.2%) patients received an endograft of bifurcated configuration, 193 (4.4%) patients received an aortouniiliac endograft, and 149 (3.4%) patients received a straight tube endograft. To assess the influence of size on the early and midterm outcome after EVAR the study cohort was subdivided according to preoperative aneurysm diameter: group A, 4.0 to 5.4 cm; group B, 5.5 to 6.4 cm; and group C greater than 6.5 cm.

Inclusion criteria, as defined in the Registry protocol, comprised elective treatment for AAA and vascular anatomy suitable for implantation of a stent graft. Baseline data including comorbidity, estimate of unfitness for open repair,[14] anatomic aspects, and operative details were recorded by the participating institutions on case record forms and were submitted for inclusion to the Data Registry Center. Findings at follow-up visits, which involved clinical examination, computed tomography (CT), or (in 5% of visits) angiography, magnetic resonance imaging, or ultrasound studies, were recorded on data forms and were returned at regular intervals to the Data Registry Center for processing and analysis. There was no outside monitoring of the centers or involvement of a core laboratory for the evaluation of CT or other imaging studies. Follow-up visits, according to the protocol, were scheduled at 1, 6, 12, 18, and 24 months, and annually thereafter. Reminders for overdue follow-up data were regularly sent to the institutions participating in the project. Outcome reporting adhered to the guidelines outlined by the Ad Hoc Committee for Standardised Reporting Practices in Vascular Surgery of The Society for Vascular Surgery/American Association for Vascular Surgery.[21] Deaths that occurred within 30 days of the initial procedure were categorised as operative deaths, and late deaths as those that occurred after 30 days. Deaths were also classified as aneurysm-related or unrelated. Aneurysm-related deaths included operative deaths and deaths that occurred as a result of aneurysm rupture, endograft infection, or within 1 month after a secondary surgical procedure to treat late complications of the aneurysm. Other outcome events observed during follow-up included endoleaks, device migration, severe device kinking, occlusion, and aneurysm growth. Only endoleaks that were identified at 1 month and thereafter were included in the analysis; endoleaks at completion angiography were not considered. Endoleaks were classified as follows: type I, or endoleaks originating from the attachment site at the proximal infrarenal aortic neck or from the distal extremity of the endograft at the level of the iliac arteries; type II, or reperfusion endoleaks from the inferior

mesenteric, lumbar, accessory renal, sacral, and hypogastric arteries; and type III, or endoleaks from the endograft itself, either from fabric damage or from connection sites between different device components. In cases in which different types of endoleaks were observed at different follow-up periods, types I and III were considered above type II for the analysis. The interval between the date of surgery and the date on which an endoleak was identified for the first time was used for life-table analysis. Aneurysm growth was determined on the recording of an increase in aneurysm diameter measured at its largest section, from outer wall to outer wall across the minor diameter on the axial CT section. Aneurysm enlargement was defined as a diameter increase of at least 8 mm relative to the preoperative measurements on CT scans. The maximum recorded aneurysm diameter during follow-up was used for this analysis, and any subsequent smaller diameter that may have occurred because of secondary treatment was omitted.

Results were reported as mean, range, and percentage of patients with discrete variables, unless otherwise specified. Preoperative patient characteristics, comorbid conditions, aneurysm anatomy at the initial procedure, and details regarding the procedure and devices were correlated with the defined study groups with univariate analysis. Differences in findings between study groups were assessed with χ^2 tests for discrete variables and with Mann-Whitney tests for continuous variables. All variables, including size classification, with a significant correlation with an adverse outcome event were entered in a multivariate Cox analysis to assess independent associations. A dichotomous categorization of used device brands was defined, with Stentor and Vanguard in one category and any other endograft in the other. This variable “device category” was entered in the model irrespective whether a significant correlation with the outcome event was found at univariate analysis. $P<.05$ was considered to represent a significant difference. Cumulative rates of freedom from aneurysm-related deaths, unrelated deaths, aneurysm rupture, conversion to open repair, and various types of endoleaks were assessed with life-table analysis. Only rates with less than 10% SE are indicated in the Results and in the figures. Significant differences between study groups were assessed with log-rank testing. All statistical analyses were performed with SAS Statistical Software (version 1.12; SAS Institute, Cary, NC).

Results

The 4392 patients, 4095 men and 297 women, ranged in age from 42 to 100 years. Average diameter of the aneurysm sac was 57.2 cm (range, 4.0-14.5 cm) in minor dimension. Group A included 1962 patients with aneurysm diameter 4.0 to 5.4 cm, group B included 1528 patients with aneurysm diameter 5.5 to 6.4 cm, and group C included 902 patients with aneurysm diameter greater than 6.4 cm. Patients in group C were on average 1.2 to 3.6 years older than those in groups A and B, more frequently had American Society of Anesthesiologists (ASA) class 3 or 4 disease, and more

frequently had cardiac, renal, and pulmonary comorbidity, compared with the other groups (Table I). Regarding existing anatomy, patients in group C had a higher incidence of significant angulation in the neck, the aneurysm, and the iliac arteries, and on average a 0.6 to 1.2 mm wider infrarenal neck. In addition, aneurysm dilatation of the common iliac arteries was more frequently observed in group C than in the other groups (Table I). Operative time was 157 minutes in group C, compared with 140 minutes in group A and 132 minutes in group B (P<.0001). Talent and Zenith endografts were significantly more frequently used in group C (Table II). Other operative aspects more frequently observed in group C included use of additional procedures (37% vs 31% in group B and 30% in group A; P=.0007) and a higher incidence of type I endoleak at completion angiography (9.9% vs 6.8% in group B and 3.7% in group A; group A vs group B, P=.001; group A vs group C, P<.0001; group B vs group C, P=.01). Primary or first-month conversion to open repair was performed in 1.1% of patients (n=21) in group A, 1.4% of patients (n=22) in group B, and 2.3% of patients (n=21) in group C (group A vs group C, P=.009; other group comparisons, not significant [NS]).

The overall first-month mortality was 2.5% (108 patients). Mortality was 4.1% in group C, compared to 2.1% in groups A and B combined (P<.0001; 2.6% in group B and 1.6% in group A). The first-month mortality in the Stentor and Vanguard category was 3.0%, and in other endografts was 2.2%, NS.

Table I. Demographic characteristics, comorbidity, and details of aortoiliac anatomy in 4392 patients

Aneurysm diameter	**Group A 4.0 – 5.4 cm (1962 patients)**	**Group B 5.5 – 6.4 cm (1528 patients)**	**Group C ≥ 6.5 cm (902 patients)**	**p-value**		
				Group A vs B	**Group B vs C**	**Group A vs C**
Age of patient (yrs + mean range)	69.7 (43-94)	72.1 (49-109)	73.3 (50-93)	< 0.0001	0.0093	< 0.0001
Male	1822 (93%)	1416 (93%)	857 (95%)	ns	0.02	0.03
ASA-class ≥ 3	944 (48%)	831 (54%)	565 (63%)	0.0002	< 0.0001	< 0.0001
Previous hx of cardiac sx or interventions	1040 (56%)	899 (62%)	588 (68%)	0.002	0.002	< 0.0001
Renal insufficiency	304 (17%)	265 (18%)	193 (23%)	Ns	0.01	0.0001
Pulmonary sx	673 (37%)	619 (43%)	400 (47%)	0.0003	0.06	< 0.0001
Diameter of infrarenal aortic neck (mm) (mean range)	22.7 (12-40)	23.3 (13-38)	23.9 (10-40)	< 0.0001	< 0.0001	< 0.0001
Significant angulation of						
- infrarenal neck	268 (14%)	392 (26%)	334 (37%)	< 0.0001	< 0.0001	< 0.0001
- aneurysm	164 (8%)	183 (12%)	137 (15%)	0.0004	0.02	< 0.0001
- iliac arteries	741 (38%)	704 (46%)	452 (50%)	< 0.0001	0.05	< 0.0001
Aneurysmatic co mmon iliac arteries	276 (15%)	271 (19%)	184 (23%)	0.003	0.0006	< 0.0001

Missing data on co-morbidity figures ranged from 220 to 318 per item; in aneurysmatic common iliac arteries, 374 missing data

Table II. Devices used in 4392 patients

	Number of devices	Group A 4.0 – 5.4 cm (1962 patients)	Group B 5.5 – 6.4 cm (1528 patients)
AneuRx	877	438 (50%)*	296 (34%)
EVT/Ancure	150	62 (41%)	56 (37%)
Excluder	341	158 (46%)	129 (38%)
Stentor	282	142 (50%)	93 (33%)
Talent	821	307 (37%)	322 (39%)
Vanguard	905	438 (48%)	295 (33%)
Zenith	891	344 (37%)	300 (34%)

Only more frequent use of brand in device groups A and C is indicated.
* P = 0.0002 more frequent use in size-group A. †P < 0.0001 more frequent use in size-group C; ^{0}P < 0.0001 more frequent use in size-group C; ¤ P = 0.004 more frequent use in size-group A.

Cardiac complications occurred in 5.6% of patients in group C, 3.3%, in group B, and 2.8% in group (group A vs group C, P=.003; group B vs group C, P=.008; group A vs group B, NS). Pulmonary complications occurred in 3.0% of patients in group C, 2.0% in group B, and 1.6% in group A (group A vs group C, P=.01; other comparisons, NS). First-month systemic complications combined were observed in 17.4% of patients in group C, 12.6% of patients in group B, and 12.0% of patients in group A (group A vs group C, P<.0001; group B vs group C, P=.001; group A vs group B, NS). There was no difference in early procedure-related or device-related complications (3.3%, 2.8%, and 2.9% in groups C, B, and A, respectively). Hospital stay was longer in groups C and B (7.0, 6.1, and 5.5 days in groups C, B, and A, respectively (group A vs group B, P=.004; group A vs group C, P<.0001; group B vs group C, P=.001).

Mean duration of follow-up was 18.4 months (range, 1-72 months), with 20.9 months (range, 1-96) in group A, 17.4 months (1-84 months) in group B, and 14.5 months (1-84 months) in group C. The difference in follow-up duration was significant (P<.0001 for any group comparison). The percentage of patients lost to follow-up after 2 years was 52% in group A, 55% in group B, and 62 in group C (NS). Patient survival was 76.0% at 5 years. Group C had significantly lower survival compared with groups B and A (62.0%, 69.6%, and 84.2%, respectively, at 5 years; group A vs group B, P<.0001; group B vs group C, P<.0001; group A vs group C, P<.0001).

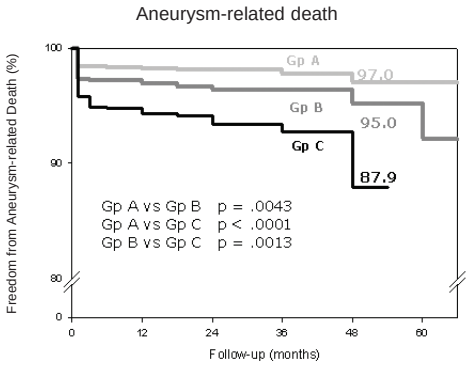

Figure 1. Cumulative freedom from aneurysm-related death. Note low attribution of survival in first 3 years of follow-up and rapid attrition in fourth year. *Gp=Group*

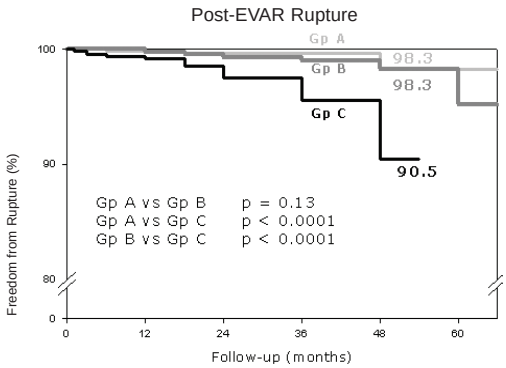

Figure 2. Cumulative freedom from rupture after endovascular aneurysm repair. *Gp=Group*

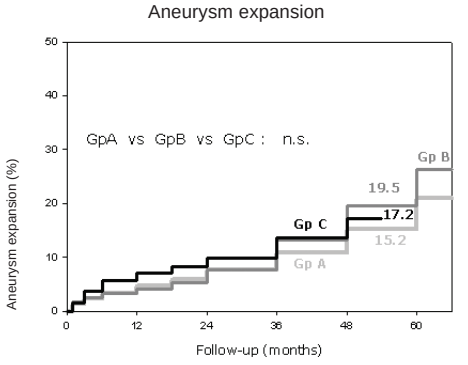

Figure 3. Cumulative proportion of patients with aneurysms growth after endovascular aneurysm repair. *Gp=Group; NS=not significant*

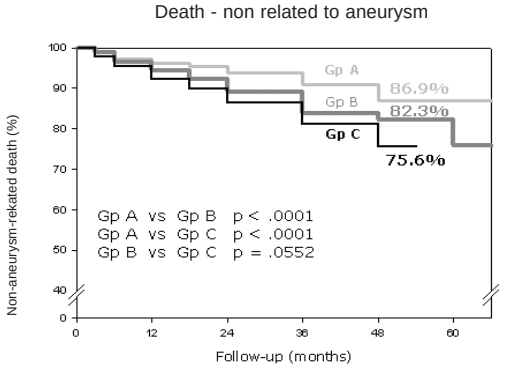

Figure 4. Cumulative freedom from unrelated death. *Gp=Group*

Aneurysm-related deaths

The freedom from aneurysm-related death in the entire study cohort was 93.9% at 5 years. Aneurysm-related deaths occurred in 53 patients in group C, 52 patients in group B, and 39 patients in group A, for a freedom from aneurysm-related death at 5 years of 87.9%, 95.0%, and 97.0% in the three groups, respectively (group A vs group B, P=.004; group A vs group C, P<.0001; group B vs group C, P=.001; Figure 1). Most aneurysm-related deaths in groups B and C during follow-up occurred in the fourth year. In group C the aneurysm-related death rate was 1% annually in the first 3 years (operative deaths not included) and 8% in the fourth year. In group B the aneurysm-related annual death rate was 0.3% in the first 3 years and 2.1% in the fourth and fifth years. This pattern can be described as a gradual increase in the first 3 years, followed

by an accelerated increase in aneurysm-related deaths in the fourth year in groups B and C (Figure 1). This trend was not apparent in group A.

Freedom from aneurysm-related deaths at 3 years stratified by device category was 95.2% in patients with Stentor and Vanguard devices and 96.9% in patients with other endografts (P=.01). Multivariate analysis indicated that large aneurysm (group C), patient age, renal insufficiency, pulmonary comorbidity, unfitness for open repair, and use of Stentor and Vanguard devices as factors with an independent correlation with increased risk for aneurysm-related death (Table III). The level of significance was less for the device category (P=0.02) than for size group C (P=.0001). A multivariate model of variables observed at follow-up, with aneurysm-related deaths omitting the first-month deaths (i.e. “late” aneurysm-related death) as outcome event indicated an independent significant correlation with large aneurysms (group C), proximal endoleak (type I), kinking of the device, and aneurysm expansion during follow-up (Table III). In this Cox model there was no correlation with use of Stentor and Vanguard device.

Table III. Risk factors for aneurysm-related death (AR), outcome of multivariate analysis

	Hazard ratio	**95% confidence intervals**
Baseline variables (early and late AR death)		
Aneurysm size, group C	2.5	1.6 - 4.0
Age	1.1	1.04 - 1.09
Renal insufficiency	1.8	1.2 - 2.7
Pulmonary condition	1.7	1.1 - 2.4
Unfit for open AAA -repair	1.7	1.1 - 2.4
Stentor or Vanguard device	1.5	1.1 - 2.3
Follow-up variables (only late AR death)		
Aneurysm size, group C	6.0	2.6 - 14.1
Type I endoleak -proximal	3.5	1.4 - 9.0
Kinking of device	3.5	1.5 - 8.3
Aneurysm growth	10.5	4.8 - 23.0

Aneurysm-related complications

Rupture post-EVAR occurred in 32 patients in the entire study cohort, with 16 ruptures in group C, 9 ruptures in group B, and 7 ruptures in group A. Freedom from rupture after 4 years was observed in 97.2% of the entire group, 90.5% in group C, 98.3% in group B, and 98.3% in group A (group A vs group B, P=.13; group A vs group C, P<.0001; group B vs group C, P<.0001; Figure 2). The rate of rupture during the study period per patient-year was 0.005 in the entire cohort, 0.015 in group C, 0.004 in group B, and 0.002 in group A. Ruptures occurred in patients who had received an AneuRx (3 of 877), Excluder (1 of 341), Stentor (6 of 282), Talent (5 of 821), Vanguard (15 of 905), Zenith (1 of 891) and “other” (1 of 108) devices. No single device brand was significantly associated with a higher risk for post-EVAR rupture. The dichotomised vari-

able of used endograft at univariate analysis was not associated with a significantly increased risk for rupture. The 3-year rate of freedom from rupture was 98.5% with Stentor and Vanguard and 99.2% with other device brands. Variables observed at follow-up that were independently associated with a higher risk for rupture included large aneurysms (group C), midgraft endoleak type III, and aneurysm expansion during follow-up (Table IV). In this Cox model the use of the Stentor or Vanguard device did not significantly correlate with rupture. Type I proximal endoleak had a higher incidence in group C (89.5% freedom from endoleak at 4 years) compared with group A (94.7%; P=.002) and group B (95.1%; P=.002). Type I distal endoleak also had a higher incidence in group C (84.9% freedom from endoleak at 4 years) compared with group A (88.7%; P=.0004). There was no significant difference between groups C and B, and groups A and B. The incidence of type III endoleaks was not significantly different in the three size groups (freedom from endoleak at 4 years, 90.3%, 87.7%, and 85.6% for groups C, B, and A, respectively). Similarly, the incidence of type II endoleaks, migration, kinking, and limb stenosis or thrombosis was comparable in the three groups.

Table IV. Risk factors for rupture of aneurysm, outcome of multivariate analysis

	Hazard ratio	**95% confidence intervals**
Follow-up variables		
Aneurysm size, group C	7.7	3.1 - 18.7
Type III endoleak	3.8	1.7 - 8.3
Aneurysm growth	4.1	1.4 - 12.1

Table V. Risk factors for conversion to open repair, outcome of multivariate analysis

	Hazard ratio	**95% confidence intervals**
Follow-up variables		
Aneurysm size, group C	1.6	1.1 - 2.3
Type I endoleak – proximal	4.0	2.7 - 5.8
Type II endoleak	2.0	1.4 - 2.9
Type III endoleak	1.7	1.2 - 2.5
Migration	1.7	1.1 - 2.5
Occlusion of limb	6.4	4.6 - 9.0
Aneurysm growth	3.9	2.4 - 6.4

Late conversion to open repair (after the first postoperative month) had a higher incidence in group C (86.2% freedom from conversion at 4 years) compared with group A (93.4%; P=.003) and group B (93.2%; P=.01). Variables observed during follow-up with an independent correlation with the decision to open conversion included large aneurysm (group C), proximal endoleak (type I), midgraft endoleak (type III), type II endoleak, device migration, limb occlusion, and aneurysm expansion (Table V). Correlation of the device category Stentor or Vanguard and conversion did not achieve significance (P .05). The incidence of aneurysm growth was not significantly different in groups C, B, and A (Figure 3).

Unrelated deaths

Freedom from aneurysm-unrelated death in the entire study cohort was 81.0% at 5 years of follow-up. Cumulative death rates due to comorbidity were significantly lower in groups B and C compared with group A (freedom from unrelated death at 4 years, 75.6% in group C, 82.3% in group B, 86.9% in group A; Figure 4). There was no statistical difference between unrelated deaths between groups C and B. In contrast with aneurysm-related deaths, there was a progressive attrition of freedom from unrelated deaths over the first 5 years of follow-up (5.8% and 4.8% annually in groups C and B; Figure 4). Of factors recorded at baseline, aneurysm size groups B and C, patient age, presence of renal dysfunction, adverse pulmonary condition, and subjective assessment of unfitness for open repair by the managing physicians had a significant independent correlation with the risk for death unrelated to aneurysm or treatment (Table VI). The use of the Stentor or Vanguard device had a borderline significant correlation with unrelated death (P=.04), as opposed to a highly significant correlation of groups C (P=.009) and B (P=.007).

Table VI. Risk factors for death not related to aneurysm, outcome of multivariate analysis

	Hazard ratio	**95% confidence intervals**
Baseline variables		
Aneurysm size, group C	1.5	1.1 - 2.1
Aneurysm size, group B	1.5	1.1 - 1.9
Age of patient	1.0	1.0 - 1.1
Renal insufficiency	1.4	1.1 - 1.9
Pulmonary condition	1.6	1.3 - 2.1
Unfit for open AAA repair	1.8	1.4 - 2.4
Stentor or Vanguard device	1.3	1.0 - 1.7

Discussion

Size of an AAA has several implications for management with EVAR. First, it was recognised that large-diameter aneurysms were less often suitable for endograft repair than smaller aneurysms.[22-24] Most frequently aortic necks were either too wide, too short, severely angulated, or these factors combined, rendering reliable infrarenal endograft fixation and sealing uncertain. However, with the newer generation of devices sealing and fixation is achievable in aneurysms that, on the basis of anatomy, previously would have been rejected for stentgraft treatment.[25-30] This is in keeping with the findings in the present study of patients undergoing EVAR. The size of the neck and angulation at several levels of the aortoiliac segment and aneurysm dila-tation in iliac arteries demonstrated a significant correlation with size groups C and B.
The correlation of larger aneurysm with a higher incidence of preoperative comorbidity is appreciable in this study. Cardiac, renal, and pulmonary conditions and generic estimates of increased operative risk, such as ASA class 3 and 4 disease and subjective assessment of patients as unfit, had a higher prevalence in patients in group C. A correlation of increased operative risk and larger aneurysm size had been observed previously.[14,16,31] Comparison of operative details in the present assessment demonstrated unfavourable outcome in large (group C) or medium-sized (group B) aneurysms in operating time, length of hospital stay, and increased rate of type I endoleaks at completion arteriography. These events are typically associated with more complex anatomy or reflected greater postoperative morbidity.[22,32,33] Moreover, additional procedures were more frequently required in group C than in the other groups.

A low perioperative mortality in comparison with conventional surgery as the benchmark has been one of the assumed assets of EVAR from the beginning of its development. A perioperative mortality of 4.1% with large aneurysms is higher than in institutional series and in the EUROSTAR series as a whole,[20,34] but still compares favourably with the mean procedural mortality of 5.5% reported in a recent review of several studies of open aneurysm surgery.[35] However, comparison of perioperative mortality rates in different series is always a dubious exercise, owing to differences in patient selection and study design.

When reporting midterm and long-term results after EVAR, it has been advised that outcome events related to the aneurysm or treatment be differentiated from events associated with preexisting comorbid factors, that is, unrelated events.[36] With regard to death rates during follow-up, a number of interesting findings came out of the present analysis. First, we noted a relatively smaller contribution of aneurysm-related death to the rate of death from all causes in the entire study cohort (freedom from death at 5 years, 94% vs 76%, respectively). Second, there was a progressive increase in both aneurysm-related and unrelated death rates with increasing aneurysm diameter. Third, the ratio of aneurysm-related to unrelated death rates demonstrated notable differences between groups, with the contribution of related deaths being largest in group C (approximately 50%, compared with 28% and 23% at

4 years in groups B and A, respectively; compare Figures 1 and 4). Thus the aneurysm-related death rate is largest in group C in an absolute sense and in a relative sense. In theory, one might conclude that the potential advantage of the minimally invasive technique becomes smaller in patients with large aneurysms, which is in agreement with previous obervations that EVAR is most durable in patients with small and medium-sized aneurysms.[37] On the other hand, one must consider that prevention of death from rupture in the vast majority in the patient category with the most unfavourable natural history and highest risk for open repair may be the best indication for EVAR.[14]

The relatively high rate of aneurysm-related midterm mortality is linked to high-risk events, such as late conversion and aneurysm rupture. The underlying cause for these events must be sought in the same unfavourable anatomic conditions that cause postoperative morbidity. In addition, a higher frequency of thrombus lining in aneurysm necks and common iliac arteries, and calcifications in the sealing zones are causes of less favourable outcome.[26,30] Although these latter characteristics were not recorded as such, because they are difficult to quantify in a multicenter registry, their importance must not be underestimated. Adverse anatomy–related findings including a significantly higher incidence of type I endoleaks of both the proximal and distal variety were more frequently observed in large aneurysms. Thus detected and undetected anatomic characteristics may account for the higher rate of rupture, conversion, and aneurysm-related deaths in patients with large aneurysms compared with medium-sized and small aneurysms.

Distribution of the various outcome events during follow-up demonstrated characteristic patterns. Unrelated deaths occurred with a relatively constant annual failure rate of 5.8% in group C throughout 5 years of follow-up. In contrast, aneurysm-related death after the first month clearly was delayed by 3 years before events occurred with higher frequency, a phenomenon that was most apparent in group C. Within the first 3 years the annual failure rate in group C was 1%, compared with an interval failure of 8% in the fourth year. If we assume that aneurysm-related death and rupture are preventable, it may be argued that after 3 years of follow-up intensified imaging surveillance may be effective for early detection of indicators of procedural failure, such as aneurysm enlargement, migration, type I or III endoleaks, device kinking, or device deterioration. These factors demonstrated an independent correlation in the multivariate analysis (Table III). Regarding intensified surveillance, one may consider more frequent follow-up visits, with precise screening of plain abdominal x-ray films, volume measurements of the aneurysm sac, and three-dimensional reconstruction of CT scans.[38-40]

Although aneurysm diameter was the main variable in this outcome study, other variables recorded either at baseline or during follow-up were assessed as potential confounders. Several variables were found to have an independent association with adverse outcome measures. Recently an increased incidence of late complications has been attributed to devices of older generations, presently withdrawn from the market.[41] In our analysis we included this variable, defined as the use of Stentor or Vanguard endografts, in the multivariate Cox models. We observed that there was an

independent correlation of old-technology endografts with aneurysm-related and unrelated deaths. However, this correlation was not so strong as the initial presence of a large aneurysm (group C) for aneurysm-related death, and medium-sized and large AAA (groups B and C) for unrelated death.

Of surprise, enlargement of the aneurysm, although correlating with rupture, conversion, and aneurysm-related death, was not associated with any of the size categories. One may only speculate why growth was not different in the size groups. Measurement of diameter in a multicenter registry is not so standardised as in a single-center study with a few CT scan readers and uniform imaging technique. While aneurysm diameter at the minor dimension of the largest diameter is part of the EUROSTAR protocol, the absence of a core laboratory to independently assess diameter measurements may enhance the lack of uniformity. To enable larger interobserver variation, a relatively large threshold of 8 mm was used to define the presence of absence of growth. Nevertheless, data accumulated in a registry no doubt will lack the accuracy of smaller studies. Third, and equally important, in many cases smaller degrees of aneurysm growth, endoleak, or migration may lead to secondary interventions before the preset threshold of 8 mm diameter increase was reached. In this regard, hard end points such as rupture and aneurysm-related death may constitute a better parameter than the more subjective measurement of diameter.

Proponents of EVAR have been criticised because they failed to clearly demonstrate any advantage of the technique with respect to protecting patients from AAA rupture.[42] In this respect, it should be noted that the risk for rupture of small aneurysms (diameter 5.5 cm) after EVAR in the present study was 0.002 ruptures per patient-year, which compares favourably with 0.008 in the similar size category in the trial arm with the initially conservative management from the UK Small Aneurysm Trial. Rupture rates per size group were calculated as Number of ruptures/(Number of patients in group mean duration of follow-up). Reduction of the risk for rupture with EVAR in medium-sized and large aneurysms as observed in the present study demonstrated, as expected, even larger differences. The rupture rate in patients in group B was 0.004, and should be compared with rates of 0.03 to 0.14, as derived from the literature in untreated aneurysms of 5 to 5.9 cm.[4-6,43] In group C we found a rupture rate of 0.015, which may be compared with 0.25 per patient-year.[4,44] Although these comparisons may not be statistically robust, it must be considered that with regard to larger aneurysms a scientifically sound assessment may not likely be performed and comparison of the outcome of different management strategies must be judged on alternative sources of information.

Post-EVAR rupture, the ultimate failure of stentgraft treatment, was observed after use of most of the device brands reported on in this registry. Analysis of many cases with post-EVAR rupture reported in the literature have revealed potentially avoidable causes, such as poor patient selection, deployment errors, or unrecognised or untreated endoleaks.[45,46] In a previous EUROSTAR publication a cumulative rupture rate of 1% per year was documented.[18] The present 0.7% annual rupture rate at 4 years in the entire series signifies some improvement, but still differs from annual cumulative

rates of approximately 0.2% found in a number of institutional series.[34,47-49] It was surprising that at our screening of articles on open AAA repair no studies were found in which the initial aneurysm diameter was included as a covariate for outcome analysis. The single exception was a study of the data for patients with primary surgery enrolled in the UK Small Aneurysm Trial.[12] It is understandable that the aneurysm diameter in this particular study demonstrated little variation (<5.5 cm), precluding a useful conclusion about a possible correlation. A comparison of the relation between aneurysm size and procedural outcome after open AAA surgery and EVAR at this time is essentially muddled by two aspects: first, the distribution of small, medium, and large aneurysms is unknown for almost any published study on open repair; and second, the respective contribution from aneurysm-related and unrelated death to the overall mortality was differentiated in few studies.[36,50] For this reason a size-stratified analysis within the randomised trials that are under way will be important.

The limitations of this study include the large number of patients who were lost to follow-up. Data for more than half of the patients after the 2-year interval were not available, despite regular reminders to participants in the study. This aspect, which probably is inherent to a voluntary registry such as EUROSTAR, may improve with the recent introduction of electronic data submission via a website. The proportion of patients with missing follow-up data was comparable in the three groups. A standard error well below 10% after 4 years is adequate for a valid assessment. However, missing data may detract from the accuracy of the cumulative event rates during follow-up.

Overall, size differences are strongly associated with adverse outcomes during follow-up. Underlying causes, such as various types of endoleak, migration, limb kinking, thrombosis, and aneurysm enlargement, correlated sometimes disparately with aneurysm size groups. However, all of these variables correlated with either end point, conversion, rupture, or aneurysm-related death, underscoring the interrelation between one another. The high incidence of medical risk factors still makes EVAR the preferred management option in most patients with large aneurysms. Old-technology stent grafts appeared important to some extent for adverse outcome, but less so than larger size of the aneurysm. Careful analysis of the causes of treatment failure remains indicated to achieve optimal long-term outcome. Until these interrelationships are better understood, intensified surveillance of patients receiving endograft treatment of a large aneurysm after 3 years of follow-up, when adverse events occur most frequently, appears a reasonable approach. With regard to patients with small aneurysms, the outcome of EVAR appears excellent. This finding may justify reappraisal of currently accepted management strategies.

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CHAPTER III

Emergency treatment of symptomatic or ruptured abdominal aortic aneurysms: the role of endovascular repair

N. Yilmaz, N. Peppelenbosch, Ph.W.M. Cuypers, A.V. Tielbeek, L.E.M. Duijm, J. Buth

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Abstract

Purpose: To report the initial experience with endovascular aortic repair (EVAR) in patients with ruptured or symptomatic abdominal aortic aneurysms (AAA) and to compare the results with conventional open surgery.
Methods: Between May 1999 and December 2001, 24 patients (21 men; mean age 75 years, range 56–89) with ruptured or symptomatic AAA underwent EVAR using a specially designed aortomonoiliac endograft. Six patients were selected based on device and operator availability; the subsequent 18 patients were treated under a modified management protocol that offered stentgraft repair to all symptomatic AAA patients. The results of this new treatment protocol were analyzed on an intention-to-treat basis for the last 8 months of the study. The 30-day outcomes in all patients treated with emergency EVAR were compared with 40 consecutive, contemporaneous patients undergoing open surgery for symptomatic or ruptured AAA.
Results: No early conversions to open surgery were performed. Significantly decreased operative blood loss and intensive care stay ($p<0.05$ for both) were observed in EVAR patients. The mortality rate for EVAR patients was 17% compared to 32% in conventionally treated patients (NS). Among patients with ruptured AAA, the 30-day mortality rates were 24% (4/17) and 41% (12/29) for EVAR and open surgery, respectively (NS). Of 26 unselected patients who were treated prospectively under the modified protocol, the majority (81%, 21/26) had anatomy suitable for endovascular repair; however, only 18 (69%) underwent EVAR owing to a short infrarenal neck (n=2) or device/operator unavailability (n=6).
Conclusions: EVAR is a feasible treatment in the majority of patients with ruptured or symptomatic AAA. The 30-day mortality appears to be similar between conventionally treated patients and those undergoing endovascular repair.

Introduction

There is now ample evidence that elective endovascular aortic repair (EVAR) is technically feasible and safe for abdominal aortic aneurysm (AAA) exclusion[1–4] ; however, ruptured AAAs pose a greater treatment challenge, and EVAR may have the potential to significantly reduce operative mortality.[5,6] Laparotomy is avoided, and the procedure can be performed under local anesthesia, which would significantly lessen the risk of a contained rupture becoming an intraperitoneal hemorrhage owing to loss of abdominal tone under general anesthesia. Additional blood loss from opening the retroperitoneal hematoma is obviated, and aortic clamping is not necessary. Additionally, cardiac stress and the duration of lower limb ischemia will be minimised. Most of these considerations apply to acute symptomatic AAAs as well, but to a lesser degree.

Since early 2000, we have treated selected patients with ruptured or symptomatic aneurysms using endovascular techniques similar to those used for elective AAA repair. From this early experience, we devised a protocol for endovascular treatment of all acutely symptomatic patients. We report our initial experience with emergency EVAR of ruptured or symptomatic aneurysms and our prospective analysis of this new treatment approach in an unselected population.

Methods

Between May 1999 and December 2001, 24 patients (21 men; mean age 75 years, range 56–89) with acute symptoms of an infrarenal AAA underwent EVAR. The diagnosis of ruptured AAA was made in 17 patients (confirmed by computed tomography [CT] in 16 and by ultrasound in 1); 12 patients were hemodynamically unstable at admission (systolic blood pressure < 100 mmHg). In the other 7 patients, a diagnosis of a symptomatic but unruptured AAA was made. Six patients were treated before May 2001 based on the availability of devices and a surgeon or radiologist experienced in EVAR. The subsequent 18 patients were treated under a modified management protocol that offered stentgraft repair to all symptomatic AAA patients. Under this protocol, which employed a 2-part aortomonoiliac (AMI) endograft system manufactured to our specifications (Medtronic AVE/Talent, Santa Rosa, CA, USA), the only exclusion criterion was anatomical unsuitability.

The management team included a vascular surgeon and/or an interventional radiologist, an endovascular-trained operating room nurse, and a radiological technician. In addition, other personnel (e.g., anesthesiologist, anesthesiology nurses, emergency department staff) were involved as appropriate for the standard management of a ruptured AAA.

The protocol involves all steps of the patient's management starting from arrival in the emergency department. Once the diagnosis of rupture is considered, fluid resuscitation is restricted, allowing the systolic blood pressure to fall to below 100 or even 70 mmHg. Only systolic pressures < 70 mmHg or cardiac arrhythmia are indications for resumption of fluid and/or blood resuscitation.

A CT scan using 150 mL of contrast (iome-prol [Iomeron 300]; BYK, Paris, France) is made with the senior surgeon in attendance to immediately assess the aortoiliac anatomy. If the infrarenal neck appears suitable for EVAR and access via one of the iliac arteries seems possible, the operating room team is notified that an endovascular repair will be performed. The entire CT scan takes 15 minutes at most, which is the time normally needed to prepare an operating room for conventional emergency surgery after the initial diagnosis of ruptured AAA is made. Standard initial steps involve establishing high-caliber peripheral venous accesses, drawing blood samples for routine laboratory studies, inserting a urethral catheter, and arranging 6 units of cross-matched blood. The patient is transferred to the operating room, and the anesthesiologist cannulates the radial artery for continuous blood pressure monitoring. Fluid management in ruptured AAA follows the rule of ‘‘as little infusion as possible’’ because increasing volume before aortic control is obtained can increase the aneurysm leak. Intravenous nitroprusside is used when needed to treat systolic pressure > 100 mmHg; fentanyl or ketamine may be used to treat pain and anxiety.

One of the femoral arteries is exposed under local anesthesia, and an introducer sheath and a guidewire (Terumo Medical Corporation, Somerset, NJ, USA) are introduced under fluoroscopic control, followed by a straight angiography catheter with multiple side holes at the tip. Angiography is performed to visualize the renal arteries. f no preoperative CT scan was made, the suitability for EVAR is obtained at this point on the basis of the angiogram. If the infrarenal neck is inadequate, a decision is taken to proceed with open surgical repair, and general anesthesia is induced.

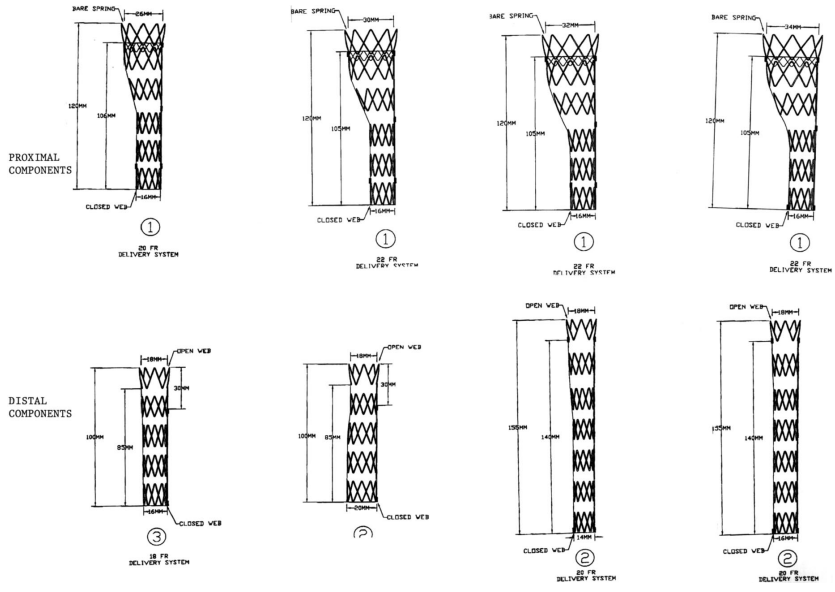

Figure 1. Aortomonoiliac configurations used for emergency treatment of ruptured AAA. Upper row represents the proximal device components and lower row the distal segments. The two longer distal limbs can be used in patients with associated CIA aneurysms, as these devices will reach to the external iliac artery for sealing.

f the infrarenal neck is suitable for a stentgraft, a delivery system containing an appropriate proximal component of the AMI device (Figure 1) is placed at the infrarenal position. The second component of the endovascular graft is deployed with its distal portion in a suitable segment of either the common or the external iliac artery. The patient is then placed under general anesthesia to perform the femorofemoral bypass and deliver an ‘‘occluder’’ (a closed stentgraft) (Medtronic AVE/Talent) into the common iliac artery (CIA) via a 16-F sheath (Cook Diagnostic and Interventional Products, Bloomington, IN, USA). Completion angiography confirms adequate fixation at the proximal and distal landing zones and identifies any endoleaks (Figure 2). All patients are admitted to the intensive care unit, where they are maintained on artificial ventilation for at least 12 hours.

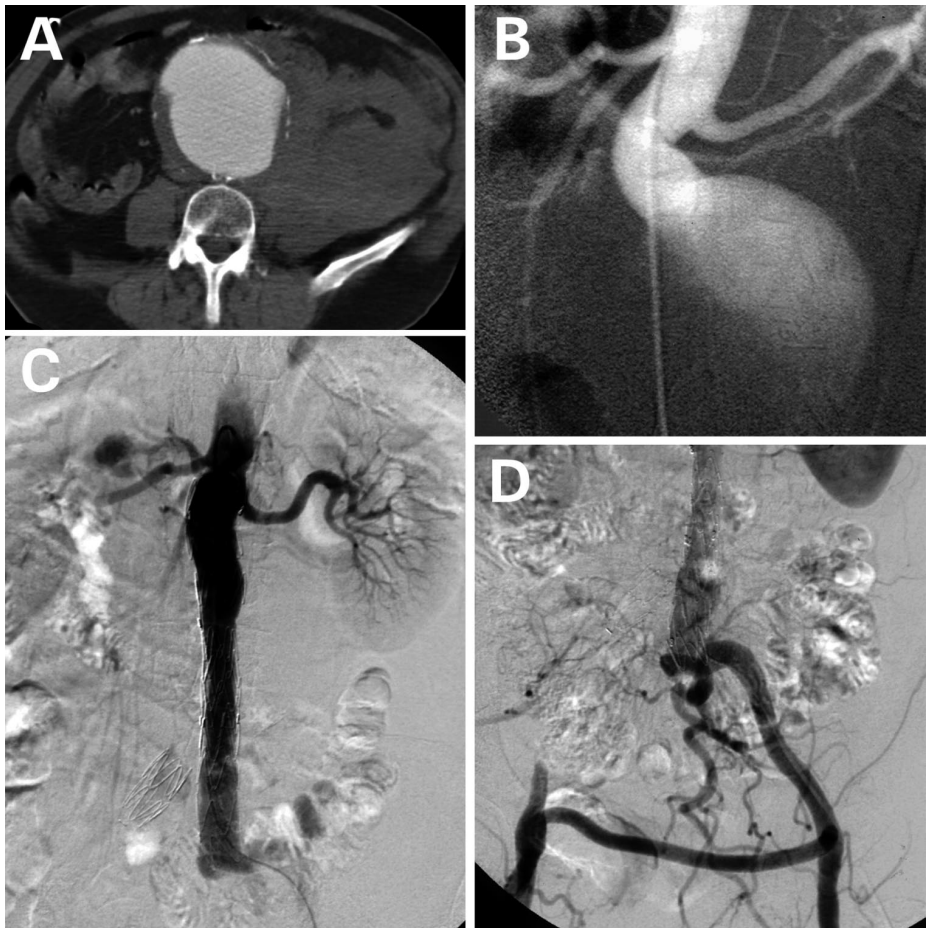

Figure 2. (A) Preoperative CT scan demonstrates perianeurysmal extravasation of blood. (B) Intraoperative angiogram. (C) Completion angiogram showing the aortomonoiliac endograft to the left iliac artery and (D) the "occluder" in the right common iliac artery.

Statistical Analysis

The initial outcome in all patients treated by emergency EVAR was assessed and compared with the results in a consecutive, contemporaneous group of 40 patients undergoing open surgery for acute symptomatic AAA. Details of exclusions and deviations from the management protocol were recorded. Early (30-day) outcome was analyzed on an intention-to-treat basis in the subgroup of unselected patients treated prospectively with EVAR. Continuous variables are presented as the mean (range). The chi-square test was used to compare outcome between groups; differences that achieve $p<0.05$ were considered significant.

Results

In the 24 emergently treated AAA patients, the AMI device was deployed in 14, while 8 received a bifurcated endograft and 2 a tube stentgraft. No conversion to open surgery was necessary. Fifteen of the 18 patients treated under the management protocol had local anesthesia for the first part of the EVAR procedure; the other 3 had spinal anesthesia. The 6 selected patients treated prior to initiation of the protocol had general anesthesia. The time in intensive care (Table I) ranged from 0 to 10 days (mean 2), and the total hospital stay averaged 15 days (2–70). Four patients required prolonged mechanical ventilation (3 owing to respiratory insufficiency and 1 with aspiration pneumonia).

Table I. Patients treated for acute AAA in a 3-year period

	Endovascular Repair (n=24)	**Open repair (n=40)**
Age (y)	75 (56-89)	73 (59-87)
Men	21 (88%)	34 (85%)
Preoperative shock	12 (50%)	24 (60%)
Ruptured aneurysm	17 (74%)	29 (72%)
30-Day mortality (entire group)	4 (17%)	13 (32%)
30-Day mortality among pati ents with ruptured aneurysm	4/17 (24%)	12/29 (41%)*
Mean operative blood loss (ml)	660 (100-1300)	3550 (300-12000+)**
Mean duration of operation (min)	173 (60-385)	237 (110-300)**
Mean hospital stay (d)	15 (2-70)	14 (1-58)
Mean intensive care s tay (d)	2.2 (1-10)	5.2 (1-50)**

Continuous variables given as mean (range); * $p > 0.1$; ** $p < 0.05$.

A large proximal endoleak, which was banded at laparotomy, was seen in the first patient of this series. Another proximal endoleak in combination with a short neck was observed in an 89-year-old patient with ruptured AAA; however, he recovered rapidly and remained without symptoms for 4 months until the study ended. A third patient developed cholecystitis and required open cholecystectomy. There were 4 (17%) deaths during the first month, all in patients with ruptured AAA (4/17, 24%): 1 multiorgan failure, 1 myocardial infarction, and 2 cases of colon ischemia in patients who had aneurysmal CIAs and bilateral hypogastric inflow obstructed by device extensions (Figure 3). The mean follow-up of surviving patients was 4 months (5–12), during which 3 patients died (1 infected endograft at 6 months and 2 unrelated causes).

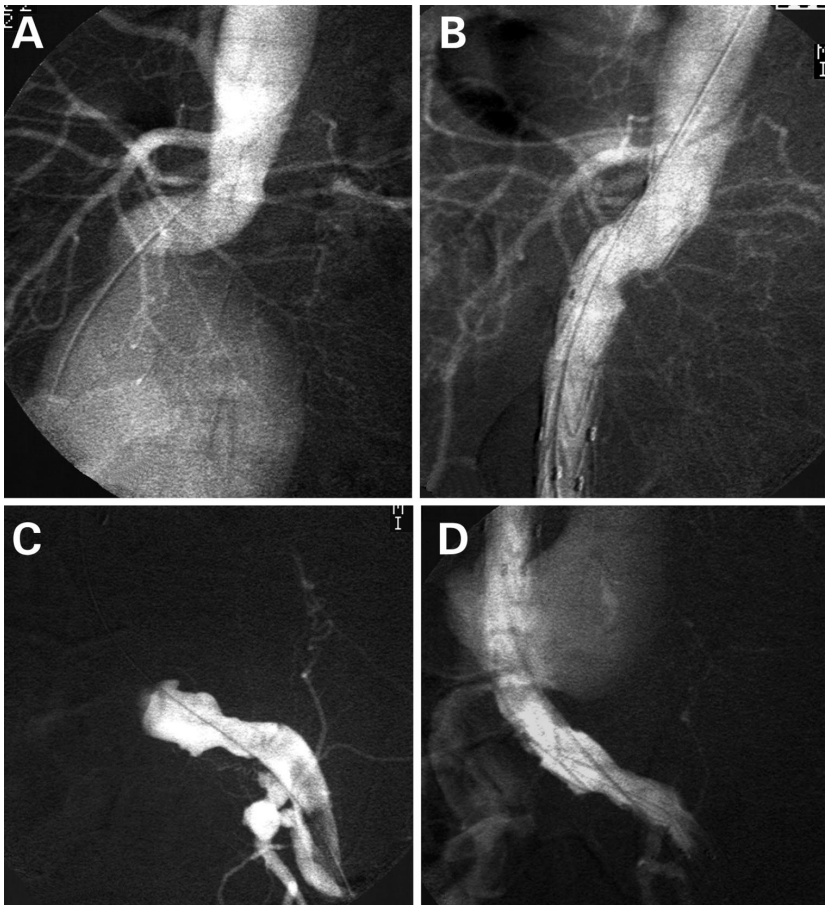

Figure 3. (A) Intraoperative angiogram demonstrating the infrarenal aneurysm neck. (B) Proximal endograft deployed. (C) Intraoperative angiogram of aneurysmal left iliac artery. (D) Endograft extending distally into the external iliac artery, obstructing hypogastric artery in-flow. The patient developed colon ischemia postoperatively.

Comparing the EVAR patients to the contemporaneous, surgically treated cohort (Figure 4A), baseline characteristics were similar (Table I). Nearly three quarters of the surgical patients (29, 72%) had rupture of their aneurysm, as documented at operation. As expected, the EVAR patients experienced less procedural blood loss and shorter intensive care stays ($p<0.05$). While the mortality rate was lower in patients treated by endovascular technique, both for the entire population and among ruptured AAA patients only, statistical significance was not achieved owing to the small groups.

In the 8 months in which the management protocol was in effect, 26 patients presented with acute AAA, of which 18 (69%) actually underwent emergency EVAR (Figure 4B). The other 8 were treated with conventional surgery owing to a short infrarenal neck in 2 patients, device unavailability in 3, and operator unavailability in another 3 cases. In these latter 3 patients, no CT scan was performed, and reliable information on suitability for EVAR was not obtained. Thus, 81% (21/26) of our prospective study AAA patients with acute symptoms were candidates for EVAR. The mortality on an ''intention-to-treat'' basis for the prospective cohort was 15% (4/26); 3 deaths were in the endovascular group and 1 in the surgically treated patients.

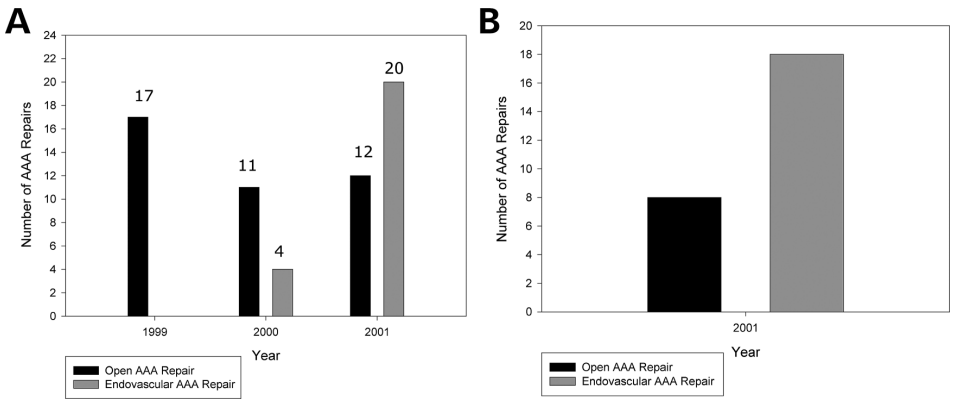

Figure 4. (A) Annual number of patients treated by open surgery and EVAR during a 3-year period. (B) Patients treated by open surgery and EVAR during the 8-month prospective evaluation of the emergency management protocol.

Discussion

Mortality rates for ruptured AAA range between 32% and 70%,[7–11] with most centers quoting rates near 50%.[12–14] This high operative mortality reflects the magnitude of the physiological stress of patients following rupture. Hemorrhage, prolonged hypotension, laparotomy, and extended lower limb ischemia all contribute to the risk of cardiac complications, multiple organ failure, and death. In addition, the patients are usually elderly and often have pre-existing comorbidities.

Ironically, the surgeon and the anesthesiologist are partly responsible for these poor results. Hypotension following rupture is frequently controlled at first by tamponade within the retroperitoneum, but relaxation of abdominal tone at induction of general anesthesia often precipitates cardiovascular collapse. Exposure of the neck of the aneurysm together with dissection through the hematoma disrupts the retroperitoneal veins and small arteries, resulting in further hemorrhage that is often difficult to control in coagulopathic patients. In the presence of a large retroperitoneal hematoma, the aorta is frequently clamped at the supraceliac segment. This renders the viscera and lower extremities ischemic, which contributes to the establishment of a fibrinolytic state[15,16] and has a dramatic effect on cardiac afterload and lactic acid production. Subsequent reperfusion of the lower limbs adds further physiological injury. Secondary bleeding episodes and other complications, such as renal failure, adult respiratory distress syndrome, and colonic and gallbladder ischemia, are ultimately responsible for most of the deaths.

Endovascular repair strongly contrasts with conventional open surgery for ruptured AAA. The endovascular approach bears similarities to recently developed principles in the management of exsanguinating injuries in poly-trauma patients. In this concept, the prime goal of the initial operation is to stop surgical bleeding as quickly as possible, using the procedure with the smallest possible injury[17] to reduce the risk of developing hypothermia, coagulopathy, and acidosis.

Endovascular repair of acute symptomatic or ruptured AAA has received little attention compared to the immense interest in EVAR for elective AAA. This is surprising, as the gain in overall survival and reduction of costs compared to open surgery might be relatively larger than in elective EVAR. After the first reported emergent case in 1994[18], it was some time before small series involving selected patients were described.[5,6,19] These studies had in common a prototype aortomonoiliac endograft made on site from standard arterial stents and conventional prosthetic materials. Aortic occlusion balloons introduced from the axillary artery were used to treat hemodynamically unstable patients. The early mortality was 16% and 45% in 2 of the reports,[5,19] but all 3 patients treated by Greenberg et al.[6] survived.

In contrast, we have used commercially manufactured AMI endografts in our more recent patients. These 2-component grafts have several significant advantages over custom-made stentgrafts, including technical ease and immediate availability without the need for preparation or sterilization. Compared to the more elaborate bifurcated endograft system, only one groin needs local anesthesia.

Perhaps most importantly, these AMI devices can be deployed quickly, which rapidly lowers intra-aneurysmal blood pressure and controls intra-abdominal bleeding. Perhaps because of our emphasis on procedural expediency, we did not need to use intra-aortic occlusion balloons in any of our patients. Their introduction via an axillary cutdown and positioning in the suprarenal aorta consumes precious time, delaying the introduction and deployment of the stentgraft, which corroborates the view described in a recent article by Hinchliffe et al.[19]

Preoperative CT scanning appears quite useful for ascertaining if endovascular treatment is feasible and for measuring anatomical dimensions. Prompt availability of CT facilities for emergency cases is essential for a successful emergency management program. When CT examination cannot be performed because of hemodynamic instability, decision-making is based on an initial intraoperative arteriogram.

Organizing a program for EVAR management of ruptured or acute AAAs is not an easy undertaking. The overall approach differs considerably from the customary care associated with conventional treatment. Important aims are to maintain systolic blood pressure < 100 mmHg, to avoid general anesthesia, and to relieve pain and anxiety. All medical and paramedical personnel need to be instructed in the protocol, but perhaps the most problematic aspect is to arrange a permanent on-call schedule of specialists with experience in EVAR. We have been able to make this arrangement by including vascular surgeons and interventional radiologists, devising a scheme in which one of these specialists is always available for emergency AAA treatment.

Our study represents an initial effort to offer EVAR to all patients with acute symptomatic aneurysms. However, logistical circumstances caused us to deviate from this policy in 6 of the 26 patients initially treated, a proportion that is likely to decrease with time. The most important observation in this study was the large percentage of acute AAA patients who were candidates for endovascular repair; only 2 patients were excluded owing to an inadequate proximal neck. Obviously, this is a small and preliminary study, which does not allow comprehensive subgroup analysis, so factors such as true rupture versus acute symptoms only, hemodynamic instability, and female gender need to be assessed in larger patient series.

Only 4 patients died in this study, all with ruptured AAAs, which was proportionally less than in the corresponding open AAA repair group. However, the endovascular procedure was directly responsible for the 2 fatal cases of colon ischemia. Both these patients had bilateral hypogastric artery occlusion because of aneurysmal iliac arteries. Although interruption of hypogastric artery inflow generally is well tolerated in elective EVAR,[20] our observations suggest that it may significantly increase the risk of colon ischemia in the setting of rupture. To avoid covering the hypogastric artery with a device limb, we have augmented our standard set of distal extensions with a ‘‘bell-bottomed’’ limb for use in large diameter iliac arteries. Other solutions to preserve hypogastric artery inflow, such as relocation of this artery,[21] seem to us too complicated for use in the emergency setting.

In conclusion, endovascular treatment is a feasible option in most of the patients presenting with ruptured or symptomatic AAA. Initial experience with this approach was encouraging, resulting in a favourably low 30-day mortality. Organizational requirements are considerable, but essential for successful implementation of a structured program for the management of this vascular emergency.

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CHAPTER IV

Emergency treatment of acute symptomatic or ruptured abdominal aortic aneurysm. Outcome of a prospective intent-to-treat by EVAR protocol

N. Peppelenbosch, N. Yilmaz, C. van Marrewijk, J. Buth, Ph.W.M. Cuypers, L.E.M. Duijm, A.V. Tielbeek

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Abstract

Objective: outcome of treatment of patients with ruptured or symptomatic non-ruptured aneurysm (rAAA and snrAAA), preferentially treated by emergency endovascular repair was assessed. The outcome was compared with a historical group of patients treated by open repair.
Patients and methods: two groups of patients presenting with acute symptomatic AAA were compared. Group I (study group) consisted of 40 consecutive prospectively enrolled patients from May 2001 until June 2002, in whom emergency endovascular abdominal aortic aneurysm repair (eEVAR) was the preferential management. Short or wide neck or profound hypovolemic shock were exclusion criteria for eEVAR. Group II (control group) consisted of 28 patients, retrospectively analysed, all treated by conventional surgical repair between January 1999 and May 2001. In group I, 26 patients had rAAA and in group II 22 patients. The other patients had snrAAA.
Results: in group I, 14 patients were treated by open repair. Unsuitable anatomy or profound hypovolemia was the cause of open repair in eight patients, while logistic reasons were the reasons for use of open repair in six patients (off-protocol use of open surgery). Thus, in this prospective series the feasibility of EVAR was 80% (32/40). Patient characteristics, proportion rAAA or hemodynamically unstable patients were comparable in group I and II. Volume of blood loss and need for fluid transfusion were significantly less in group I compared to group II. The perioperative mortality in group I was significantly less than in group II (20% vs. 43%, respectively, p=0.04). If patients with rAAA were considered the mortality was 31% in group I and 50% in group II, which difference did not reach the level of statistical significance.
Conclusion: eEVAR was a feasible treatment in the majority of patients with rAAA and snrAAA. Blood loss and the requirements of fluid transfusion were significantly decreased. Most importantly in this institutional series significantly lower first-month mortality was observed in the group with preferential eEVAR compared to a control group. A multicenter study assessing the outcome of preferential use of eEVAR in patients with acute symptomatic AAA is required.

Introduction

A ruptured aneurysm of the abdominal aorta (rAAA) is the 6th leading cause of acute death in the US.[1] The only treatment that may save a patient's life consisted of emergency surgery with replacement of the ruptured aorta by a vascular prosthesis. Most published data indicate a perioperative mortality of conventional open surgery, which ranges from 32 to 70%.[2-8] In a recently published paper a gradual reduction of the operative mortality over time was demonstrated until a current rate of 41%.[9] During the previous decade the development of endovascular abdominal aortic aneurysm repair (EVAR) has changed the practice pattern of elective treatment in asymptomatic patients considerably. EVAR has become a routine procedure in many institutions, although statistical evidence of decreased perioperative mortality is currently not available. Nevertheless, it is considered by many the treatment of choice in patients with increased risk of conventional open surgery. In emergency repair of patients with symptomatic non-ruptured abdominal aortic aneurysms (snrAAA) stentgraft treatment may have several advantages compared to an open procedure. One aspect is the use of local anaesthesia rather than general anaesthesia. It is believed that the induction of general anaesthesia, which is associated with the loss of arterial sympathetic tone, frequently causes complete circulatory collapse in a patient with severe hypovolemia and compensated shock. In addition relaxation of the abdominal wall may cause a contained retroperitoneal rupture to turn into an open intraperitoneal haemorrhage. The operative and perioperative mortality increase dramatically with massive blood loss in patients with a free intraperitoneal rupture.[2,3] The type of anaesthesia may be one of the reasons of a possibly better outcome in endograft-treated patients with ruptured AAA.

In the present report an analysis of our experience with emergency-EVAR (eEVAR) is presented. This work differs from a previous preliminary publication from our institution in that more patients were included and the study group has been redefined.[10, 1] The objective of the present study involved the assessment of the outcome of treatment in a consecutive group of patients with symptomatic or ruptured AAA. This approach allowed us to evaluate (1) the applicability of eEVAR, and (2) the possible impact of eEVAR on the early mortality in an unselected cohort of patients with acute symptomatic aneurysms.

Methods

From May 2001 onward, patients with symptomatic snrAAA and rAAA of the abdominal aorta presenting at the Catharina Hospital, Eindhoven, The Netherlands, were treated according to a well-defined management protocol involving intent-to-treat by eEVAR. Aneurysms were considered symptomatic non-ruptured (snrAAA), if there were no CT signs of haemorrhage outside the wall of the aneurysm, but with acute pain in the abdomen and an abdominal aneurysm, which was painful at palpation. Aneurysms were

defined ruptured (rAAA) if there was extravasation of blood surrounding the aneurysm at CT examination. In patients that did not undergo CT examination a retro-peritoneal haematoma at open surgery was the criterion for rupture of the aneurysm. During the study period all patients who were referred to our hospital with a symptomatic aneurysm of the abdominal aorta, were prospectively analysed and included in this study.

On arrival in the emergency ward the intravenous fluid infusion rate was minimised. The protocol involved that patients were taken to the radiology department for emergency CT examination with intravenous contrast infusion to opacify the aorta. An exception was made for patients in profound shock (systolic blood pressure < 60 mmHg not responding to rapid infusion of fluid) or who had a cardiac arrest during transportation to the hospital, diameter and length of the infrarenal neck of the aneurysm were measured and the decision whether endovascular repair was feasible was taken and communicated with the operating room staff. Exclusion criteria for eEVAR were a short neck (less than 10 mm length), a wide neck (over 30 mm in diameter) and inaccessible iliac arteries. Following CT examination patients were quickly transported to the operating room for the selected emergency procedure, or taken to the intensive care unit (ICU) for further optimalisation (only in snrAAA). Patients with rupture of their aneurysm were preferentially treated with an aorto-uni-iliac endograft, combined with a crossover bypass (Figure 1). Details on the devices used were described in a previous paper of our group.[10]

The study group described above was compared with a control group of patients with a symptomatic aneurysms, who were treated by open procedure, between January 1999 and May 2001. This historical control group was retrospectively analysed by hospital chart review. Primary outcome events that were compared included: 30-day or in-hospital mortality, morbidity, length of hospital and ICU stay, intraoperative blood loss, requirement of blood products and overall fluid infusion during operation.

The follow-up protocol consisted of routine CT-scanning at 1, 3, 6 and 12 months and hereafter every year for patients treated with eEVAR. Patients treated by open surgery were seen back after 1 month and 3 months, hereafter yearly. Patients sent in from other hospitals were readmitted back and have the same schedule.

Statistical analysis was performed using SPSS® for Windows® version 9.0. Chi-square and Fisher tests were used for the comparison of discrete variables and the Mann-Whitney test was used for continuous variables. Continuous variables are presented as the mean (range). A p-value of <0.05 was considered significant.

Account of patient cohort in the present study and control group relative to previous publication[10]

Of the 24 patients treated with eEVAR in the previous assessment six were not considered in the present study as they consisted a pilot phase and were selected on favourite aspects. The cohort with consecutive enrolment with intend-to-treat by EVAR was increased by eight EVAR patients (44% of previous EVAR group), while 14 patients treated by open surgery enrolled under the same protocol were also included for a total of 40 patients in the study group. Six of these 14 patients were new enrolled

patients since the previous study.
The previous article included 40 patients with open surgery of which eight felt within the intend-to-treat by EVAR study period. Four additional patients with open surgery were excluded (one because he had a suture-line aneurysm and three with snrAAA because they had been admitted longer than 24 h before treatment), for a total of 28 patients constituting the present control group of consecutive enrolled patients use open surgery.

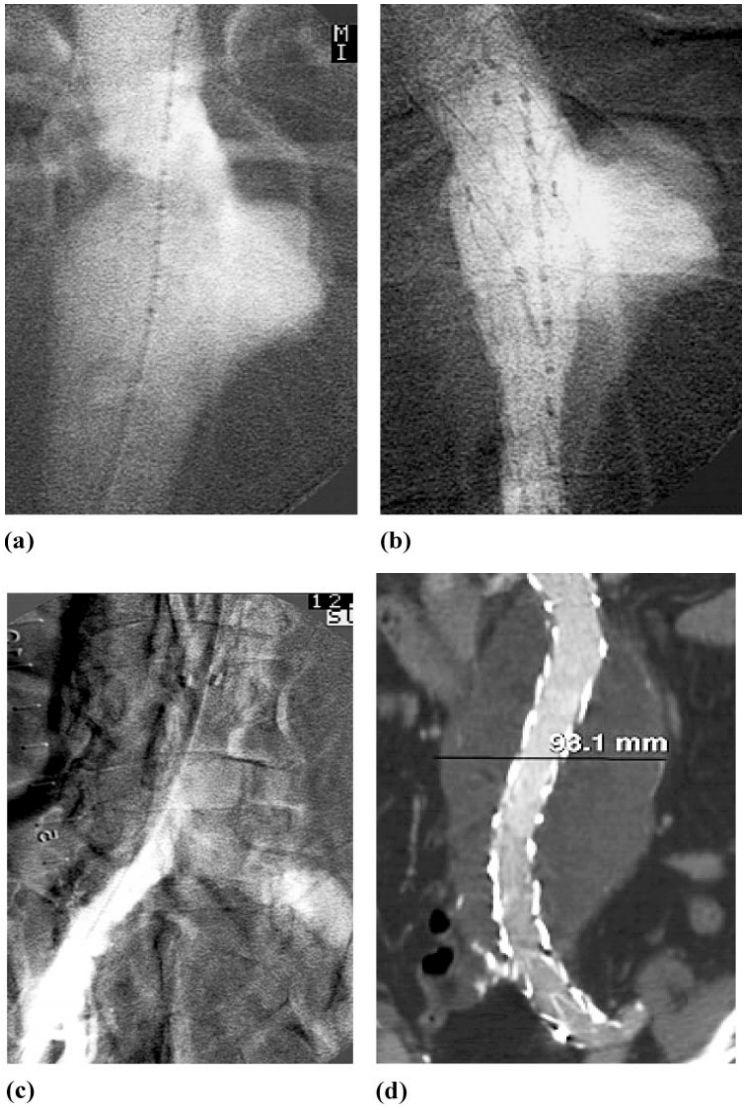

Figure 1. (A) Intraoperative angiogram demonstrating ruptured AAA. (B) Intraoperative angiogram demonstrating deployment of proximal component of aorto-uni-iliac device. (C) Intraoperative angiogram demonstrating bilateral iliac arteries. (D) Postoperative CT-examination, demonstrating functioning aorto-uni-iliac device with complete exclusion of the aneurysm.

Results

Patients

From May 2001 until June 2002, 40 consecutive patients in the study group were admitted and treated in our hospital because of a ruptured or symptomatic infrarenal abdominal aneurysm (group I, Table I). Twenty-six patients received endovascular repair (EVAR subgroup), and 14 patients conventional open surgery (COS subgroup, Table II). There was a trend that patients in the conventional group were hemodynamic less stable and had larger aneurysms, however, these group differences in patient characteristics were not significant (Table II). The control group with routine open repair consisted of 28 patients treated between January 1999 and April 2001 (group II). There were no significant differences with regard to patient characteristics, presence of preoperative shock or previous cardiac and/or pulmonary events, between group I and II.

Table I. Patient characteristics in group I and II

		Group I Study group (40 patients)	**Group II Control group (28 patients)**
Male/female	N	34/6	22/6
Mean age (range)	Years	73.0 (56.8-90.0)	73.2 (58.1-86.7)
SnrAAA/rAAA	N	14/26	6/22
Mean ∅ AAA (range)	cm	7.0 (3.6 – 10.0)	7.5 (4.0 – 10.5)
Systolic < 100 m mHg	N (%)	16 (40)	14 (56)
History Cardiac events	N (%)	12 (30)	9 (32)
History Pulmonary events	N (%)	7 (18)	6 (21)

Table II. Patient characteristics of subgroups in group I (40 patients)

		Subgroup with EVAR (26 pts)	**Subgroup with COS (14 pts)**
Male/female	N	23/3	11/3
Mean age (range)	Years	74.1 (56.8-90.0)	71.0 (58.2-80.9)
SnrAAA/rAAA	N	10/16	4/10
Mean ∅ AAA (range)	cm	6.7 (3.6 – 8.8)	7.7 (5.0 – 10.0)
Systolic < 100 mm Hg	N (%)	8 (31)	8 (57)
History Cardiac events	N (%)	8 (31)	4 (29)
History Pulmonary events	N (%)	6 (23)	1 (7)

In the study group 14 (35%) patients had snrAAA and 26 (65%) a rAAA, in the control group 6 (21%) patients had a snrAAA and 22 (79%) a rAAA (Table I). The differences were not statistically significant. Of the patients with a snrAAA two of the control group and two of the study group were taken to the ICU and treated within 24 h with an urgent operation. All other 16 snrAAA patients were treated without delay by emergency operation.

In the study group 33 (83%) patients underwent an emergency CT-scanning. Seven patients did not undergo CT-scanning, three in the EVAR and four in the COS subgroup. Reasons for not performing a CT-scanning were profound hypovolemic shock (in two patients) and logistic reasons in five patients. All these patients were immediately transported to the operating room. In the three patients who received eEVAR fluoroscopic assessment was performed with calibrated catheters to establish the diameter of the neck and neck length. In case open surgery was performed fluoroscopic assessments were not performed. The mean neck length was significantly longer in the EVAR subgroup compared with the COS subgroup, 18.0 (6-36) and 7.5 (0-15) mm, respectively (p=0.004). The neck diameter in the two subgroups was not statistically different, 23.8 (17-33) and 27.8 (20-34) mm in EVAR and COS, respectively.

Applicability of eEVAR

EVAR was performed in 26 patients of the 40 patients in the study group. Reasons for COS were unavailable endovascular specialists in six patients and unsuitable anatomic (dimensions of the infrarenal neck, five patients), or technical (profound hypovolemia, three patients), reasons in eight patients. Thus the feasibility of EVAR based on an acceptable aortoiliac anatomy and hemodymanics was 80% (32/40). The overall applicability of eEVAR in this study was 65% (26/40).

Procedural details

The intraoperative and hospital aspects in group I and II are summarised in Table III. In the EVAR subgroup no conversions to open surgery were required. Most often an aorto-uni-iliac device was used in combination with a femorofemoral crossover bypass (19 patients). Two patients received a tube-endograft and five received a bifurcated stentgraft. Of the patients who received a bifurcated stentgraft two had snrAAA. In 25 patients, a Talent® stentgraft was used. In one patient a bifurcated Excluder® stentgraft was used. In 88% of the cases in the EVAR subgroup, either local (in 15 patients) or regional (in eight patients) anaesthesia was used. Two patients with snrAAA and one with a rAAA received general anaesthesia. The patient with ruptured aneurysm was in deep hypovolemic shock at arrival in the hospital. It was felt by the responsible anaestesiologist that in this patient a more rapid control of the hemodynamic situation might be obtained by general anaesthesia. Mean operation time was 155 (80-270) min in group I, and 176 (100-240) in group II, which was not a significant difference. Mean blood loss in group I was 1800 (100-1600) ml, and in group II 3900 (300-12000) ml.

This difference was statistically significant (p=0.01). in addition, there was a significant difference between group I and II with regard to total fluid infusion (blood components, fresh frozen plasma and crystalloids combined; p=0.004). Administration of blood components was comparable in the two groups.

Table III. Intraoperative and hospital characteristics in group I and II

		Study group (40 patients)			Control Group (28 pts)
		Total (40 pts)	EVAR (26 pts)	COS (14 pts)	
Mean operation time (range)	Minutes	155 (80-270)	154 (80-270)	155 (90-240)	176 (100-240)
Anaesthesia					
Local		15	15	-	-
Regional		8	8	-	-
General		17	3	14	28
Technique performed					
Tube		11	2	9	21
Bifurcated		10	5	5	7
AUI + crossover		19	19	-	-
Mean blood loss (range)	ml	1800 (100-6000)*	1100 (100-2500)	2600 (500-6000)	3900 (300-12000)
Mean fluid infusion (range)	ml	6600 (1500-20500)†	4700 (1500-12500)	10400 (3400-20500)	9000 (5000-13700)
I.C.U. stay (range)	Hours	81 (0-408)	46 (0-220)	154 (12-408)	122 (11-864)
Hospital stay (range)	Days	12.3 (0-60)	7.2 (0-21)	22.1 (1-60)	13.0 (0-59)

* $p < 0.01$; † $p < 0.004$ (numbers indicate patients unless stated otherwise)

Perioperative morbidity and mortality

The hospital and ICU stay in the study group and control group was not statistically different (Table III). The perioperative mortality rate in the study group with preferential EVAR was significantly lower than in group II, 20 and 43%, respectively (p=0.04, Table IV). If only patients with rupture of their aneurysms were considered the mortality rate in group I was 31% and in group II 50%. This difference did not reach the level of statistically significance (p=0.10). Causes of death included continued bleeding, cardiac failure, multi organ failure, respiratory insufficiency and bowel ischaemia. The latter constituted 50% (two patients) of the causes of death in the EVAR subgroup. The rate of postoperative morbidity among survivors was in the study group higher than in the control group (44% versus 25%, respectively) (Table IV). However, this difference did not reach statistical significance.

Table IV. Mortality and Morbidity in group I and II

		Study group (40 patients)			Control Group (28 pts)
		Total (40 pts)	EVAR (26 pts)	COS (14 pts)	
Mortality	(%)	8 (20)*	4	4	12 (43)*
Cardiac		2	-	2	2
Pulmonary		-	-	-	1
Continued bleeding		2	1	1	1
Multiorgan failure		2	1	1	4
Bowel ischaemia		2	2	-	3
Postoperative morbidity	(%) of	14(44)**	8	6	4(25)**
Cardiac	survivors	2	2	-	-
Pulmonary		3	1	2	1
Multiorgan failure		1	-	1	-
Coagulation disorder		-	-	-	2
CVA		1	1	-	-
Re-operation		3	-	3	1
Wound haematoma/infection		4	4	-	-

* p = 0.04; **p = 0.3

Follow-up of patients

In the EVAR subgroup, three patients demonstrated an endoleak during follow-up from 30 days to 14 months: two patients had a type I and one patient a type II endoleak. The latter patient is still under survey and an intervention for coiling has been planned. Both patients with type I endoleak refused further intervention because of their age of, respectively, 90 and 80 years. The 90-year old patient has a follow-up time of 14 months and he remains without symptoms. The 80-year old patient was discharged from further follow-up on his own request.

Follow-up was achieved in 90% of the patients in the study group and 86% in the control group. The patients, with recorded follow-up data, were followed in the hospitals from were they origionally were refered. The six-month survival in group I was 74% and in group II 52% (Figure 2). This difference of 22% already existed after the first post-operative month and there was no further change of this difference in the subsequent follow-up period.

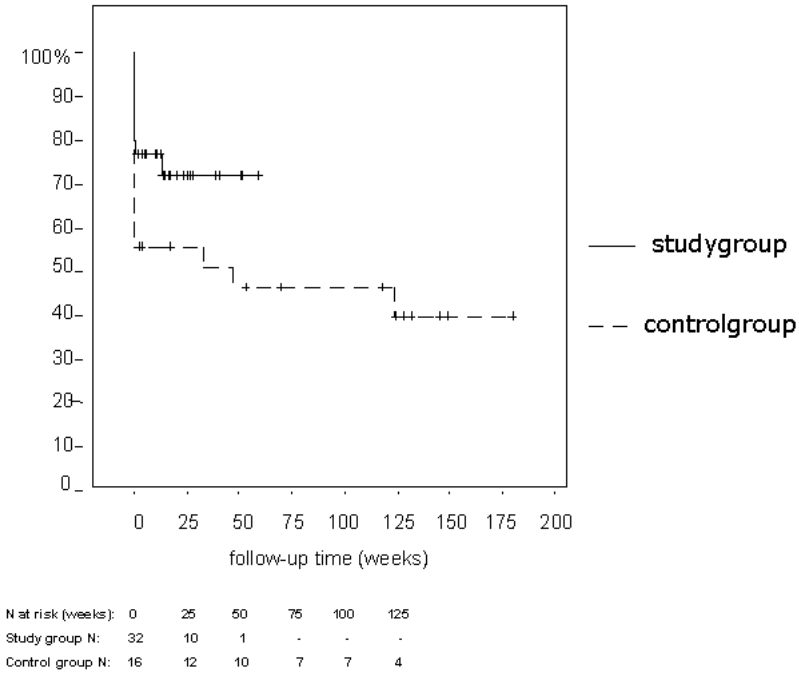

Figure 2. Kaplan-Meier survival curves of patients in the study group and in the control group. Initially existing difference sustains during the first month of follow-up. Numbers indicate patients at risk.

Discussion

Conventional open surgery has been the gold-standard for the treatment of acute symptomatic aneurysms for five decades.[11] During this period the perioperative mortality and morbidity has improved only modestly.[2-9] After the successful introduction of elective stentgraft repair of asymptomatic abdominal aneurysms,[12-15] this technique now also is considered appealing for the treatment of acute symptomatic aneurysms.[11,16,18] Mortality rates in these studies range from 10 to 45%, which is promising considered the prohibitive mortality in open surgery. However, none of these studies was based on an intention-to-treat by EVAR protocol or on a consecutively enrolled patient group. Rather, patients were selected on the basis of availability of experienced staff and other practical aspects. Also in the previous report from our group, Yilmaz assessed the outcome in a consecutive series with regard to the treatment received, patients with EVAR versus open repair. In the present series, the larger and redefined study group allowed to assess the overall impact of eEVAR.

In the present study, group I consisting of both patients with EVAR and COS and group II including patients with open surgery, demonstrated less difference in preoperative characteristics than in our previous study because of redefined study groups. No differences in operating time and ICU admission time were noted between group I and II. Patient selection criteria for EVAR involved in the first place the presence of a suitable infrarenal neck. This was apparent in the study group from a significantly shorter neck in the subgroup with COS compared to the subgroup with EVAR.

The use of local rather than general anaesthesia may be one of the important factors determining outcome of treatment.[17] in our study group, 58% received local or regional anaesthesia. These types of anaesthesia do not influence the tone of the abdominal wall. Relaxation of the abdominal musculature during general anaesthesia may change a contained rupture into an intraperitoneal or free rupture, reducing the change of survival significantly.[3] Local anaesthesia has the additional advantage of leaving the sympathetic tone of the arterioles unchanged. Patients with ruptured AAA usually are in a state of compensated shock with maximal vasoconstriction. Release of the sympathetic tone at induction of general anaesthesia may cause complete cardiovascular collapse, as most of the surgeons know from practical experience. Reduction of blood loss and fluid administered during operation in the EVAR subgroup are likely related to the avoidance of general anaesthesia as much as to avoiding open surgery.

Preoperative CT-scanning on the one hand appears quite useful for ascertaining whether endovascular treatment is feasible, and for measuring anatomical dimensions. A drawback may be the time delay until the treatment commences. In the present series only two patients had too low blood pressures to allow an additional delay of 10-15 min, which is the usual time an emergency CT-scan takes in our institution. During CT-examination the operating room is prepared for the operative procedure, making the actual time delay even less.

The use of an aorto-uni-iliac rather than a bifurcated endograft is a matter of debate. During our institutional experience we have developed a strong preference for AUI-endografts. The advantage of this device type include a quick introduction and deployment, which rapidly lowers intra-aneurysmal blood pressure and provides control in the intra-abdominal bleeding.[19] Only one groin needs to be explored under local anaesthesia, which seems more easily tolerated by the patient in emergency circumstances than bilateral groin exploration. An additional advantage of AUI grafts seems that patients with complex iliac artery anatomy can more frequently be treated by aorto-uni-iliac devices as only one suitable side is needed. Nevertheless, Orend et al. and Lachat et al. used bifurcated stentgrafts in their selected patient population with comparable operating times and excellent results.[16,17]

To demonstrate the impact of endograft treatment on the first-month mortality of acute AAA requires a careful analysis. Simple assessment EVAR-treated patients will lead to a skewed outcome, as patients with short necks or in profound shock will have the highest risk, but will be excluded for EVAR. It is of note that the present study is also the first to demonstrate a significant difference in first-month mortality in favour of

eEVAR compared to conventional surgery in a combined group of patients with ruptured and symptomatic AAAs. The advantage of eEVAR continues during the first postoperative months. Apparently there is no catch-up of mortality by delayed events and the favourable effect on survival seems durable. Admittedly, our present follow-up periods were still rather short. It is of note that the incidence of postoperative complications among survivors in group I was somewhat higher than in group II. A plausible explanation may be that the occurrence of complications in the first group was assessed prospectively and in the latter retrospectively. Nevertheless, this finding also may indicate that complications occur in patients with eEVAR that may cause death when open surgery would have been performed.

The present study has several flaws. First, a relatively small number of patients were included and the follow-up period was short. Secondly, despite the intent-to-treat by EVAR protocol six patients (15%) received conventional open repair because of an unavailable endovascular specialist at the time of admission. When these patients also would have been treated by EVAR, the difference in early mortality might have been even greater. Thirdly and perhaps most importantly, the control group in this study was analysed retrospectively, which may influence the comparability with the study group as well as accuracy of recording events. A large scale multicenter study is needed to confirm, that emergency EVAR for acute symptomatic and ruptured aneurysms is associated with improved survival. Once our findings are confirmed by such a study, additional evidence will be required from a randomised controlled trial comparing EVAR and open surgery for clearly delineated indications, distinguishing patients with truly ruptured and symptomatic non-ruptured AAA. The importance of a trial monitoring committee that terminates the study as soon as a statistically significant difference in operative survival is obtained at regular interim analyses is obvious in such a RCT.

Late complications associated with eEVAR incuded the occurrence of endoleaks. In the present study three endoleaks (12%) of survivors were present after one month. Two patients had a type I proximal endoleak, but refused further treatment. So far they remained without symptoms. Nevertheless, these endoleaks in our opinion should be treated either by the use of a giant Palmaz-stent, an aortic extension endograft or by laparoscopic banding of the aorta. The policy in type II endoleaks may be similar as in elective EVAR and intervention should be dependent in eventual increase in size of the aneurysm.[20]

In conclusion, emergency endovascular repair of ruptured and acute symptomatic abdominal aortic aneurysms is justified when the patient has a suitable anatomy, most importantly an adequate infra-renal neck. The first-month mortality in the present study was significantly lower than in a control group receiving surgical repair. Further study of a larger study population to confirm our findings is needed.

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CHAPTER V

Emergency endovascular treatment for ruptured abdominal aortic aneurysm and the risk of spinal cord ischemia

N. Peppelenbosch, Ph.W.M. Cuypers, A.C. Vahl,
F. Vermassen, J. Buth

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Abstract

Background: Spinal cord ischemia is a rare complication after open surgical repair for ruptured abdominal aortic aneurysms (rAAA). The use of emergency endovascular aortic aneurysm repair (eEVAR) is increasing, and paraplegia has been observed in a few patients. The objective of this study was to assess the incidence and pathogenesis of spinal cord ischemia after eEVAR in greater detail.
Methods: This was a retrospective analysis of patients who had eEVAR for rAAA in three hospitals in The Netherlands and Belgium during a 3-year study period that ended in February 2004. The use of aortouniiliac devices combined with a femorofemoral crossover bypass was the preferred technique. Patients with postoperative symptoms of spinal cord ischemia were identified and the influence of potential risk factors was assessed. These factors included the presence of common iliac artery aneurysms necessitating device limb extension to the external iliac artery with associated overlapping the hypogastric artery, the prolonged interruption of bilateral hypogastric artery arterial inflow during the procedure (defined “functional aortic occlusion time” >30 minutes), and the occurrence of preoperative hemodynamic shock.
Results: Thirty-five patients were treated by EVAR and they constituted the study group. The first-month mortality in the study group with EVAR was 23%. Four patients (11.5%) with EVAR developed paraplegia postoperatively; the unilateral or bilateral hypogastric artery in all four patients became occluded during the procedure. In the other 31 patients who did not have paraplegia, the unilateral or bilateral hypogastric arteries became occluded in 14 patients (45%). This constituted a significant difference in the prevalence of hypogastric artery occlusion in patients with or without paraplegia (P=.04). The functional aortic occlusion time was prolonged in all four patients with paraplegia and in five without spinal cord ischemia (P=.0003). All four patients with spinal cord ischemia presented with hemodynamic shock. This factor did not reach a significant difference from nonparaplegic patients.
Conclusion: Emergency EVAR continues to be a promising approach to reduce the high mortality of rAAA, but the incidence of spinal cord ischemia after endovascular treatment of rAAA was worrisome. Although the pathogenesis is most likely multifactorial, interruption of the hypogastric artery inflow appeared to have significant influence. In patients with aneurysmatic common iliac arteries, any effort should be made to minimize hypogastric occlusion time during the procedure and to maintain hypogastric artery inflow afterwards, either by the use of a bell-bottom iliac extension or by electing open repair.

Endovascular repair is increasingly used as an alternative to open surgical repair of ruptured abdominal aortic aneurysms (rAAAs). Emergency endovascular aneurysm repair (eEVAR) keeps the promise that it is associated with lower operative mortality and morbidity than open surgery. A reduction in blood loss and length of intensive care unit stay has been observed in a number of nonrandomised clinical studies. The operative mortality in these studies varied between 0% to 25%,[1-10] which compares favourably with the mortality rate of 40% to 50% that is usually reported for patients treated by open surgery.[11-13] However, the clinical experience until to date is limited, and published series included only four to 37 patients. Despite a favourable initial experience, several issues associated with eEVAR have not been fully assessed. For instance, the risk of branch ischemia affecting the bowel, the lower limbs, and the spinal cord may be different from acute surgical repair of the aneurysm. Of these events, spinal cord ischemia is a rare complication in series with open repair of rAAA, with an incidence varying from 1% to 2.8%.[11-13] Until recently, paraplegia after emergency endovascular treatment has only been reported in a single case.[14] We recently observed this complication in a few additional patients, and this caused us to assess the incidence, risk factors, and consequences of spinal cord ischemia after eEVAR. In the present report, we have reviewed the 30-day outcome of eEVAR experiences from three institutions. The previously reported case is included in the present series.

Material and methods

The experience with eEVAR was prospectively recorded in three hospitals in The Netherlands and Belgium. These institutions were Catharina Hospital, Eindhoven, and Onze Lieve Vrouwe Gasthuis, Amsterdam, The Netherlands, and University Hospital, Gent, Belgium. In this report, hospitals will be indicated by the name of their city. The clinical information was collected and entered in a database to be assessed retrospectively as a combined patient series. The inclusion period in Eindhoven was from May 2001 until February 2004; in Amsterdam, from January 2003 until February 2004; and in Gent, from February 1997 until February 2004.

Selection criteria of patients for eEVAR differed between hospitals. Preferential treatment of patients by eEVAR was used in Eindhoven[15] and Amsterdam. In these centers, the anatomic suitability for EVAR was the primary determinant for stentgraft repair. In Gent, selection for eEVAR was based on available staff and time of presentation in addition to a suitable anatomy. Only patients that were actually operated were taken into account. Patients who died before the operation started were excluded, as were patients with previous endovascular or open aortic procedures and those with suprarenal or thoracoabdominal ruptured aneurysms and dissections.

The written protocols in the three centers were that upon the patient's arrival in the emergency department, the intravenous fluid infusion rate was minimised and an emergency computed tomography (CT) examination was performed. For the diagno-

sis of a rAAA, the preoperative CT examination was required to demonstrate extravasation of blood. Diameter and length of the infrarenal neck of the aneurysm were measured, and the decision on whether endovascular repair was feasible was made and communicated with the operating room staff. After the CT examination, patients were quickly transported to the operating room for the selected emergency procedure.

In endovascularly treated patients, the preferred operative technique in rAAA consisted of an aorto-uni-iliac (AUI) graft. The reasons for this preference, which are shared with other groups, have been described previously. The main arguments include a greater application rate of the stentgraft technique because of fewer anatomic restrictions and a quicker decompression of the bleeding aneurysm.[1,2,7,8,15] AUI endografting was combined with a crossover bypass. Standard emergency sets of AUI stent grafts and distal extender iliac device limbs (Talent, Medtronic, Santa Rosa, Calif) were permanently available in the three centers.

Emergency EVAR commenced under local anesthesia of the groin at the selected access side. The rational for using local anesthesia in the initial part of the procedure has been described previously by our group and by others.[15,16] The main purpose is to avoid a severe circulatory collapse associated with the induction of general anesthesia in the patient with extensive retroperitoneal bloodloss.[17] After introduction of an angiography catheter, the renal arteries were visualised, delineated, and marked on the fluoroscopy screen. This was used as a guide to deploy the proximal part of the AUI set. Next, the distal component of the stent graft to the selected iliac artery was positioned and deployed. Sealing within the common iliac arteries was preferred. However, in case of a common iliac artery aneurysm, the external iliac was the landing site and the hypogastric artery (HA) inflow was inevitably sacrificed in this process. Occasionally HA coiling was used for obliteration and prevention of type II endoleaks, but most frequently this was done by ligature, or no coiling was performed.

At this point of the procedure, general anesthesia was induced and the contralateral common femoral artery exposed. This artery was used for introduction of the occluder device into the common iliac artery. The operation was completed by performing a crossover femorofemoral bypass. A completion angiogram was used to check for endoleaks.

Patients who demonstrated symptoms of spinal cord ischemia after the eEVAR procedure were examined by neurologists. Their consultation notes were used to classify the neurologic status of the patients according to the categories described by Gloviczki et al.[18] In this classification, type I involves complete infarction of the distal spinal cord, type II is also known as the anterior spinal artery syndrome in which proprioception is saved, and types III to VI represent different patterns of infarction of lumbosacral nerve roots and segmental or patchy infarctions of the spinal cord.

Several factors were examined for correlation with the occurrence of postoperative development of spinal cord ischemia:

1. The presence of preoperative and intraoperative hemodynamic shock. Shock was defined as a systolic blood pressure of $\leq$ 90 mm Hg.

2. Permanently blocked HAs. HA inflow after EVAR was either antegrade, retrograde, or blocked. In cases where an endograft or an occluding plug did overlap the HA, the inflow was considered to be blocked. Antegrade inflow was present in endografts when the side of the landing was in the common iliac artery. Retrograde flow was present on the side of an occluding plug in the common iliac artery contralateral to an AUI device (Figure 1).
3. Temporary interruption of HA flow during the procedure. To determine the effect of interruption of HA inflow on the risk of paraplegia, "functional aortic occlusion time" was defined to indicate the duration of interrupted inflow to both internal iliac arteries. The functional aortic occlusion time will be prolonged in patients with a common iliac artery aneurysm ipsilateral to the AUI endograft. To exclude the aneurysm, the device limb needs to seal in the external iliac artery and will occlude the ipsilateral HA. During the procedure from this point in time, bilateral HA occlusion exists.

Figure 1. Magnetic resonance angiogram of ipsilateral (right) hypogastric artery occlusion and retrograde perfusion of the contralateral (left) hypogastric artery.

After a number of subsequent operative steps, including exposure of the contralateral the common femoral artery, deployment of the occluder plug, and construction of the femorofemoral bypass, the retrograde flow to the contralateral HA is established and pelvic ischemia is terminated. Prolonged functional aortic occlusion time was arbitrarily defined as an interruption of inflow to both HAs of > 30 minutes.

Statistical analysis was performed using SPSS version 9.0 software (SPSS Inc, Chicago Ill) for Windows (Microsoft, Redmond, Wash). The χ^2, Fisher's exact, and Mann-Whitney U tests were used as appropriate, depending on whether the variables were discrete or continuous and on group size. Variables were presented as means and ranges. P<.05 was considered significant.

Results

Patient details and treatment outcome

Thirty-five patients with rAAA were treated by eEVAR and constituted the study group. This group consisted of 31 men and four women with a median age of 73 years (53 to 89 years). Patients' ages were comparable in the three participating institutions, and men predominated (Table I). The study group of 35 was part of an overall group of 101 patients treated for rAAA during the study period, for an eEVAR in rAAA application rate of 35%. This rate varied considerably between institutions. In Eindhoven, 22 of 39

patients underwent eEVAR for a 56% application rate of eEVAR in rAAA; in Amsterdam, it was four (36%) of 11 patients; and in Gent, it was nine (18%) of 51 patients. The 66 patients who did not receive eEVAR were treated by open surgery.

The mean length of hospital stay in the study group was 10 days (0 to 82 days). The 30-day mortality was 23% (8 patients). In comparison, the first-month mortality in the patients with open surgery was 29% (19 patients). There was no difference in the 30-day mortality, severe morbidity, and length of hospital stay in EVAR-treated patients among the institutions (Table I). The causes of death in the study group included continued hemorrhage, bowel ischemia, and multiorgan failure. Ten of the surviving patients (37%) had the following severe postoperative complications: pneumonia (3 patients), myocardial infarction or congestive heart failure (3 patients), cerebrovascular accidents (1 patient), and other adverse events (3 patients). Four patients (11.5%) had postoperative paraplegia, and these patients will be discussed in detail in the next section.

Table I. Patient characteristics of the study group

	Total	Eindhoven	Gent	Amsterdam
Patients	35	22	9	4
Male/female	31 / 4	18 / 4	9 / 0	4 / 0
Age (years, median and range)	73 (53 - 89)	75 (61 - 88)	70 (53 - 89)	74 (72 - 77)
Hospital stay (days, median and range)	10 (0 - 82)	14 (0 - 82)	15 (5 - 62)	10 (6 - 33)
Severe morbidity of survivors	10 (37%)	6 (35%)	2 (22%)	2 (50%)
First month mortality	8 (23%)	6 (27%)	2 (22%)	0 (0%)

Table II. Postoperative patency of hypogastric arteries

Device configuration	Total	Bilateral HA open	Antegrade flow blocked (ipsilateral* HA occlusion)	Retrograde flow blocked (contralateral$^{\nabla}$ HA occlusion)	Bilateral HA occlusion
Aorto-uni-iliac device	32	15$^{\lozenge}$	4**	8	5***
Bifurcated device	3	2	1	--	--

HA = hypogastric artery; * Ipsilateral to the side of the aorto -uni-iliac stent graft in four patients; in one patient with a bifurcated stent graft, a HA was occluded; $^{\nabla}$ Contralateral to the side of the aorto -uni-iliac stent graft; $^{\lozenge}$ One patient has bypasses to both Has after overlapping by device limbs; ** Two patients became postoperatively paraplegic; *** Two patients already had one HA occluded preoperatively.

Preoperative hemodynamic shock was present in 20 patients (57%) in the study group. AUI endografts were used in 32 patients (91%). HAs were postoperatively occluded in 18 patients (51%) because of overlapping by the distal device component (Table II). In all cases, this was necessitated by aneurysmatic dilatation of the common iliac arteries

> 28 mm, except in one patient in whom HA ligation was required because of iliac artery kinking (see next section). In one patient with bilateral HAs overlapping a bypass, revascularization was performed during the initial procedure to both HAs. This patient was counted in the analysis as having open HAs. The functional aortic occlusion time was prolonged in the nine patients (26%) who had ipsilateral HA overlapping (mean, 52; range, 38 to 70 minutes).

Patients with paraplegia

In four (11.5%) of the 35 patients, paraplegia developed 10 to 96 hours after the procedure. No patients with open repair during the study period had symptoms of spinal cord ischemia (P=.13). In three of the patients with spinal cord ischemia, spinal fluid drainage was instituted (Table III). Partial neurologic improvement in sensory function and rectal tone was observed in one patient after spinal fluid drainage. The spinal cord ischemia was classified as type I in two patients and as type II in the other two. Two of the patients with spinal cord ischemia died within the first month from multiorgan failure. None of the patients had symptoms of peripheral arterial emboli.

Three patients with spinal cord ischemia had AAA diameters of 75 to 117 mm, and one patient had an iliac aneurysm of 55 mm in diameter. All four patients had hemodynamic shock preoperatively, were treated with an AUI device, and had either an ipsilateral or bilateral HA occlusion during the procedure (Tables II and III). In one patient, the occlusion of the ipsilateral HA resulted from ligation and division of this artery that had been performed to resolve a severe kinking and obstruction of the stented iliac artery (Figure 2).

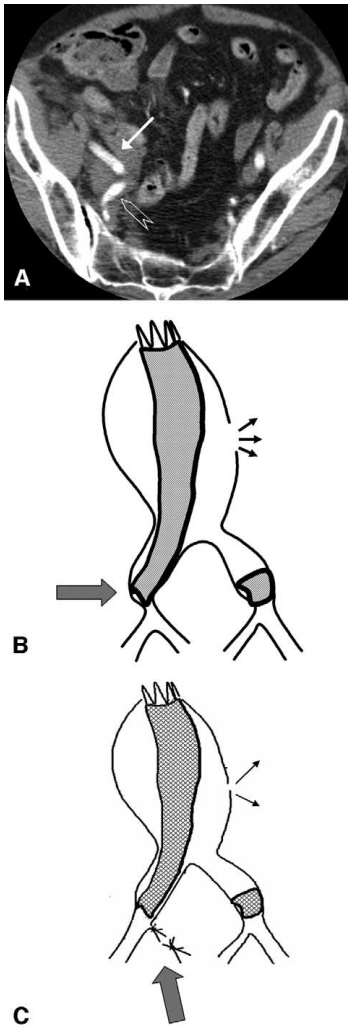

Figure 2. **A**. Same patient as in Fig 1. Preoperative computed tomography examination demonstrated on the right side severe iliac kinking at the hypogastric artery origin. External iliac artery indicated by a white arrow and the hypogastric artery by an open arrow. **B**. Schematic visualization of the mechanism of severe kinking of iliac artery causing an occlusion of aortouniiliac stent graft. Large arrow indicates obstructed stentgraft outflow. Small arrows indicate site of aneurysm rupture. **C**. When the right hypogastric artery was ligated (arrow), the kinking was relieved and flow to the extremity was re-established; however, this patient became paraplegic after the procedure.

Correlation of several risk factors demonstrated that HA occlusion and prolonged functional aortic occlusion time were the only significant variables associated with spinal cord ischemia (P=.04 and P=.0003, respectively) (Table IV). Statistical correlation with unilateral or bilateral HA occlusion and with occlusion ipsilateral or contralateral to an AUI endograft demonstrated no significant differences, perhaps because of the small size of these subgroups. In patients without spinal cord ischemia, preoperative shock was observed in 52%, 90% were treated with an AUI device, and 10% had coexistent occurrence of colon ischemia.These three variables had no significant correlation with paraplegia. Consequences of spinal cord ischemia involved a higher risk of postoperative death (50% vs 19% of patients without this complication, P=.04).

Table III. Patient characteristics of the patients with spinal cord ischemia

Patient	Age	Ø AAA	Lowest RR systolic	Hypogastric arteries	Type II endoleak	Spinal tap procedure	Classification Of SC (type)	Neurological improvement	Outcome
A	77 y	7.7 cm	55 mmHg	Bilateral occluded*	Yes	Yes	I	No	Survived
B	84 y	7.5 cm	65 mmHg	Ipsilateral Occluded	No	Yes	I	Yes	survived
C	71 y	5.5 cm**	55 mmHg	Ipsilateral occluded	Yes	Yes	II	No	Died$^{\nabla}$
D	70 y	11.7 cm	55 mmHg	Bilateral occluded	No	No	II	No	Died$^{\lozenge}$

SCI = Spinal cord ischemia; * Ipsilateral hypogastric artery was preoperatively alrea dy occluded. After occlusion Type II endoleak was present ; ** Ruptured iliac aneurysm ; $^{\nabla}$ Patient died of respiratory insufficiency ; $^{\lozenge}$ Patient died of pulmonary embolism

Table IV. Univariate correlation of clinical variables and spinal cord ischemia

	All patients N = 35 (%)	Without spinal cord ischemia N = 31 (%)	With spinal cord ischemia N = 4 (%)	p-value
Preoperative hemodynamic shock (systolic blood pressure < 90 mmHg)	20 (57 %)	16 (52 %)	4 (100 %)	0.18
Prolonged functional aorta occlusion time (>30 min)	9 (26%)	5 (16%)	4 (100%)	0.0003
HA occlusion (any)	18 (51 %)	14 (45 %)	4 (100 %)	0.001
HA occlusion by overlapping stent -graft	4 (11 %)	2 (6 %)	2 (50 %)	0.31
HA occlusion on site of Occluder plug in case of AUI-device	9 (26 %)	9 (29 %)	-	0.30
Bilateral HA occlusion	5 (14 %)	3 (10 %)	2 (50 %)	0.89
Colon ischemia	3 (9 %)	3 (10 %)	-	0.7
Use of AUI endografts	32 (91 %)	28 (90 %)	4 (100 %)	0.9

Data are given as number (percentage) of patients in each group unless stated otherwise. AUI device: aorto-uni-iliac stentgraft. HA: hypogastric artery

Table V. Publications on patient series with emergency endovascular repair of ruptured abdominal aortic aneurysm

First author	*Year*	*Patients (n)*	*AUI or bifurcated stent graft*	*Hypotensive (%)*	*Mortality (%)*	*Postoperative SCI (%)*	*Occlusion of HAs (n)*
Okki[1]	2000	20	AUI	31	10	0	17 unilat
Hinchliffe[2]	2001	18	AUI	20	45	0	2 unilat/1 bilat
Orend[3]	2002	21	Bifurcated	33	14	0	NA
Verhoeven[4]	2002	9	Bifurcated	NA	11	0	NA
Van Sambeek[5]	2002	4	Bifurcated	0	0	0	NA
Resch[6]	2003	21	AUI	24	19	0	NA
Reichart[7]	2003	6	AUI	31	17	0	NA
Lee[9]	2004	13	Bifurcated	0	8	0	NA
Heckelhammer[10]	2005	37	Bifurcated	22	11	0	NA
Present series	2005	35	AUI	57	23	11.5	13 unilat/5 bilat

AUI: Aortouniiliac device; SCI: spinal cord ischemia; NA: not applicable

Discussion

The first-month mortality of 23% in this series of patients with endovascular treatment of their rAAA was in agreement with the mortality rates observed in previous studies on eEVAR[1-10] and compared favourably with the results of open surgery. However, in the patients receiving open surgery during the study period in the three participating institutions, a comparable mortality of 29% was observed. Because the present series, similar to any of the previous studies on eEVAR, was retrospective in design, one may conclude that the outcomes of prospective randomised studies need to be awaited before a better comparison of the mortality rates can be made. Meanwhile, the evolving clinical experience allows us to study the pattern of complications in patients receiving eEVAR.

Paraplegia is a severe complication of aortic surgery with the highest incidence after surgical repair of thoraco-abdominal aneurysms, in particular those with Crawford's classification II and III.[19] Ischemic neurologic injury to the spinal cord or the lumbosacral plexus after operations on the abdominal aorta is reportedly more frequent after surgical repair of ruptured aneurysms,[20] although the incidence in large series varied from only1% to 2.8%.[11-13] The use of endovascular techniques for the elective management of infrarenal AAA was also associated with a low incidence of spinal cord ischemia. In a study by EUROSTAR of 2862 patients, six (0.21%) developed postoperative spinal cord ischemia.[21] A few additional reports on paraplegia after elective EVAR have meanwhile appeared.[22,23] Only 149 patients with emergency stent-graft repair for rAAA were accounted for in the previous literature (Table V).[1-10] There were no reported patients with postoperative paraplegia in any of the previous series. Differences in patient selection for eEVAR in these studies may preclude an accurate

comparison of the incidence of spinal cord ischemic injury with the present study group. As a result of our preference to use eEVAR in all anatomically eligible patients, the present study included approximately twice as many patients with severe hypotension than any of the previous studies. In addition 50% in our series had a common iliac artery aneurysm, which constitutes an issue with important interventional complexity implications. In most of the previous studies, the occurrence or treatment of this complexity was not discussed. These aspects indicate the selection of patients with a higher-risk profile in the present series. Nevertheless, the relatively high rate of spinal cord ischemia of 11.5% was the main reason for our analysis.

In the etiology of spinal cord neurologic deficit after open abdominal aortic aneurysm procedures, the following risk factors have been indicated:

1. Interruption of the arteria radicularis magna, often called the artery of Adamkiewicz. The variable anatomy of this artery makes it vulnerable to inadvertent blockage, not only with supraceliac clamping, but also with infrarenal clamping.[24]
2. The interruption of collateral pathways via the HAs and the inferior mesenteric artery. The malperfusion of the pelvic arteries is more frequently associated with the risk of colon ischemia. However, pelvic ischemia is increasingly recognised as a contributing factor of spinal cord ischemia.[25-27]
3. The severity and duration of preoperative and intraoperative hypotension, and
4. Aortic embolization, may lead to spinal cord infarction.

Most authorities in this field consider that spinalcord ischemia after abdominal aortic operations is likely multi-factorial and may involve interference of multiple of the above etiologies.[24,28] The occurrence of paraplegia after implantation of endovascular aneurysm devices may be associated with somewhat different etiologic factors. Severe hemodynamic shock with systolic blood pressures < 65 mmHg was present in all four patients with paraplegia in our report. A difference with patients receiving open surgery may be the time delay to the operation because of the CT examination required for the stentgraft procedure. This may prolong the duration of shock. The average time delay may be relatively small, as CT scanning usually took 15 minutes and was performed during the preparation of an operating room. We assume that a longer hypotensive period only was of significance in conjunction with other factors.

Embolization of atheromatous debris caused by the catheter procedures or introduction of the endoluminal device may also be a potential cause of spinal cord ischemia. However, the incidence of embolism after elective EVAR is low, and in our patient group, there were no symptoms of peripheral emboli.

Aortic clamping as a technical, routine procedure in open surgery is not used in EVAR. However, in patients with common iliac aneurysms treated by endovascular implantation of an AUI stent graft, the procedure was associated with overlapping of the ipsilateral HA in nine patients (26% of the study group). Despite the advantages of the AUI technique over the bifurcated endograft, indicated in the methods section, a potential disadvantage may include a longer time period before arterial flow is reconstituted in the HA contralateral to the AUI device. This period of pelvic ischemia,

which was defined as functional aortic occlusion time, is determined by the time needed to explore the contralateral groin, place the occluding plug in the contralateral iliac artery, and perform the crossover femorofemoral bypass. The mean functional aortic occlusion time was 51 minutes, which seems only slightly longer than the usual time of infrarenal aortic clamping in open surgery. Nevertheless, a prolonged functional aortic occlusion time appeared to be a significant factor to spinal cord ischemia, and we must conclude that the duration of HA inflow interruption during the procedure should be minimised.

Permanent obstruction of HA inflow appeared another significant cause of the spinal cord ischemia in our patients. In four, the ipsilateral HA became occluded, and two had also occlusion of the contralateral HA. The cause in all patients was device limb extension to exclude a common iliac artery aneurysm > 28 mm, except in one patient in whom the HA was ligated to release kinking. From this series, the evidence is lacking to clearly demonstrate a greater importance of maintaining antegrade inflow of the ipsilateral HA compared with retrograde inflow of the contralateral HA in case of use of an AUI device. We did not have information on hypogastric secondary branch arteries in this series. However, previous studies have demonstrated their importance.[27,29] We assume that frequent occlusion of HAs using the stentgraft technique for rAAA treatment compared with open surgery may be part of the explanation of a higher prevalence of paraplegia after eEVAR in our series. Most publications on eEVAR have not indicated the rate of HA overlapping, precluding a comparison with the present series. The precise incidence of HA inflow interruption with open surgery could not be retrieved from the literature. However, this will probably be lower than with eEVAR in the present series.

It seems important to maintain hypogastric inflow in emergency endovascular management of patients with ruptured AAA. In case of aneurysmatic common iliac arteries, we now use bell-bottom iliac device limbs to land in the least aneurysmatic common iliac artery proximal to the level of the HA.[30] When this is not possible, as in case of bilateral extensively aneurysmatic common iliac arteries, conventional open surgery may be safer than a stentgraft procedure.

Weaknesses of this report included the retrospective nature of the study and the fact that in one of the centers, eEVAR use was partly based on logistic factors rather than on anatomic factors only.

Conclusion

Although eEVAR continues to be a promising approach to reduce the high mortality of rAAA, the prevalence of spinal cord ischemia after endovascular repair of rAAA combined with HA inflow interruption is worrisome. The duration of inflow interruption of the HAs during the procedure should be restricted. In the case of a common iliac aneurysm, the use of a bell-bottom iliac extension should be considered to avoid blockage of HA blood flow.

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CHAPTER VI

Endograft treatment in ruptured abdominal aortic aneurysms using the Talent® AUI stentgraft system
Design of a feasibility study

N. Peppelenbosch, S. Zannetti, B. Barbieri, J. Buth
On behalf of the ERA study collaborators

Eur J Vasc Endovasc Surg 2004; 27:366-371

Abstract

Objectives. To study the outcome of patients with ruptured AAA treated by EVAR using the Talent® AUI stentgraft system.
Design. A multicenter prospective consecutive patient cohort of 100 patients.
Materials. Consecutive patients with ruptured AAA will be screened for treatment by EVAR. All patients screened, including those excluded from EVAR, will be clustered and called the study group. The study group will be compared with a historical group of patients with ruptured AAA derived from literature. The New ERA study started February 2003.
Outcome. Main outcome events are applicability rate and operative mortality rate of the study group.
Conclusion. The study rationale and design are reported here.

Background of the Study

Abdominal aortic aneurysms (AAA) larger than 5.5 cm have a significant risk of rupture, which dramatically increases with aneurysms with diameter over 6.5 cm.[1,2] Open surgical repair has typically been associated with an inhospital mortality rate of approximately 50% (40–70%).[3–5] Only a slight improvement in the outcome of ruptured (r) AAA over time was documented in a recent meta-analysis (3.5% reduction per decade), and the mortality rate as achieved in 2000 was estimated at 41%.[6] A number of non-randomised studies suggest that for elective AAA treatment, endovascular aneurysm repair (EVAR) is associated with a lower (major) morbidity and stress response than open surgery.[7–11] The reduction in major morbidity may give an improvement in out-come in patients with ruptured aneurysms given the far higher mortality in rAAA treated with conventional open surgery.

Previous Publications

Emergency (e) EVAR has been assessed in a limited number of studies.[12–17] The mean number of patients treated by eEVAR for a documented ruptured infrarenal AAA in these reports was 15 with a range of 4–21 patients. The mean first month mortality rate in these series was 17% (range 0–45%). However, it was disconcerting that only two reports indicated that their series consisted of consecutively enrolled patients, rendering the outcomes in the other reports strongly influenced by selective patient recruitment. Patients selected for eEVAR likely constitute a lower risk category, as they would need to be stable for preoperative imaging and have a suitable anatomical configuration. Thus the good outcomes in these studies may simply reflect selection bias.

An additional point of concern was the applicability rate of eEVAR. In studies that did indicate the proportion of patients with rAAA that received eEVAR, this rate varied from 27% to 78%.[12–14,16,17] While the concept of eEVAR will lose much of its appeal if it can only be applied to the minority of patients, one must take into account that the criteria of eligibility were based on those customarily used in elective EVAR. However, it may be appropriate to consider less stringent anatomical criteria in patients with rAAA, in particular larger infrarenal neck diameters. Elective repair of AAAs with large neck diameters has not been associated with an increased incidence of proximal endoleak.[18] Rigid application of industry imposed criteria and overly cautious application, well justified in elective AAA-repair, seems counterproductive in emergency treatment of rAAA.

Rationale for Study Design

The New ERA study was conceived to allow an assessment of the feasibility of eEVAR. All patients presenting with rAAA within a study period and not only the sub-

set treatable by EVAR will be included. In addition, this consecutive series with preferential eEVAR (the study group) will be compared with a comparable historical cohort that was treated by conventional open surgery.

A randomised comparative trial (RCT) to assess the value of eEVAR for rAAA would be ideal. However, in our opinion a RCT conducted at the present time, would be biased against the endo-technique. These biases include: the influence of a learning curve, an insufficiently developed infrastructure for rapid pre-operative imaging and a quick execution of an emergency endovascular procedure in hospitals, traditionally familiarity with urgent open aneurysm repair and insufficient number of endovascular specialists available for on-call rostas. A non-randomised cohort study with preferential eEVAR allows the opportunity for a comparison of the primary outcome events with the outcome of up to date meta-analysis and to resolve any organisational issues within the study centers.

Organisation of the Study

The New ERA study is a prospective, multicenter, feasibility European and Canadian study that is sponsored by Medtronic® and supported by the Medtronic® Bakken Research Centre. The objective is to evaluate applicability, clinical performance, safety and effectiveness of stentgraft placement in rAAA using the Talent® AUI stentgraft system. Vascular surgeons and interventional radiologists with considerable experience in the diagnosis and treatment of rAAA have been included as investigators in this study (list of participating investigators is reported in Appendix A). Patient data and procedural details are recorded in structured Case Report Forms (CRFs), periodically monitored by the organising company. Adverse events are reported to and evaluated by an Adverse Event Advisory Committee. Some of the members in this committee represent the Medtronic company (AEAC, members of AEAC are reported in Appendix B). Study conduct is supervised by the Steering Committee (Appendix C) consisting of representatives of Medtronic® and clinical professionals.

An adverse event (AE) is any undesirable clinical occurrence in a patient whether or not related to the device. Any change in nature, severity, or degree of a pre-existing condition is also recorded as an AE. An SAE is recorded if the patient's hospitalization is prolonged or the patient requires re-admission, another intervention or dies. Twelve centers will participate in this study. The evaluation of the study objectives requires 100 patients, each with a follow-up of 3-months. The study has started in February 2003. A consecutive series of patients treated for ruptured infrarenal abdominal aortic aneurysms (rAAA) is included in the study, in each of the participating institutions. The preferential treatment will be EVAR, open surgery is only selected as treatment when anatomic criteria preclude effective exclusion of the aneurysm, or if the patient is in profound hypovolemic shock that does not allow pre-operative CT scanning or the use of intravascular ultrasound to evaluate EVAR feasibility. Included in the study are patients treated by stentgraft technique or, in the case of adverse

anatomy for endoluminal stentgrafting, by open surgery. Patients who are suitable for EVAR will be treated with the aorto-uni-iliac (AUI) Talent® stentgraft system (Figure 1).

The Talent® stentgraft configuration consists of a 2-piece AUI with interchangeable proximal and distal components, for 'off-the-shelf' customisation with variable diameters and lengths. The 2-piece AUI configuration potentially reduces the complexity of the procedure compared to a bifurcated design, contributing to quicker aneurysm exclusion.

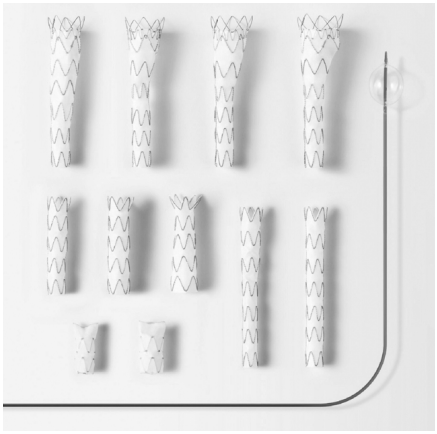

Figure 1. The components of the Talent® aorto-uni-iliac stentgraft system used for emergency EVAR

Purpose and Objectives

The purposes of the New ERA study are:

1. to assess the proportion of patients, presenting with rAAA in whom EVAR is applicable;
2. to determine operative mortality and morbidity in a cohort of patients treated with EVAR, when possible.

Study endpoints include: operative mortality, defined as death within the first 30 days or duringthe same hospitalisation and major morbidity (i.e. serious adverse events). Secondary endpoints include: death from all causes and aneurysm-related death, both within three months after the procedure.

Patient Selection, Inclusion and Exclusion Criteria for the Study

During the study period each participating center will enrol a series of consecutive patients with a rAAA that meet the inclusion criteria. Rupture of the aneurysm is defined as haemorrhage outside the aortic wall, documented by preoperative CT-examination, pre-operative ultrasound, or in case of a laparotomy by direct observation. In the case that there is still doubt after treatment whether the AAA was ruptured, rupture is to be confirmed by postoperative CT-scan or by autopsy. The patient, or his/her relatives are informed about the study and asked permission to participate by a written informed consent. The criteria for enrolment in the study, and after enrolment, eligibility for EVAR, are summarised in Table I.

Table I. Inclusion and exclusion criteria for the New ERA study

Inclusion criteria
Age > 50 years
Patients with documented rupture of the infrarenal aorta (preoperative CT, preoperative ultrasound, laparotomy, postoperative CT -scan, autopsy)
Written informed consent by patient or legal representative
Exclusion criteria
No documentation of true rupture
Rupture because of endoleak of a stentgraft placed *before* the study has started
Severe dementia
Active infection
Malignancy with life expectancy less than one year
No consent to p articipate in the study
Deliberate decision of the patient (or representatives) to be treated by open surgery

Triage of Patients that Meet the Inclusion Criteria

Patients in stable haemodynamic condition, or with mild to moderate haemodynamic instability (systolic blood pressure > 60 mmHg and no severe cardiac arhythmia) undergo CT-examination. Arrangements for CT-examination without any delay and short transportation time between the emergency ward, the CT-department and the operative department are prerequisites for participating institutions (Figure 2—flow sheet).
Severely unstable patients in profound hypovolemic shock that does not allow CT-scanning (i.e. systolic blood pressure < 60 mmHg and/or repeated requirement for cardiac massage due to severe cardiac arhythmia) are taken to the operating room and clinically evaluated and if possible undergo fluoroscopic assessment to establish whether an EVAR or open surgical procedure can be performed.

The anatomic criteria determining treatment by open surgery include an infrarenal aortic neck length smaller than 10 mm and/or a diameter larger than 32 mm. In addition, an angulation of the infrarenal neck larger than 85° excludes the patient from EVAR. Bilateral iliac artery occlusions or stenosis (< 6 mm diameter), not amenable to balloon angioplasty, represent exclusion criteria for EVAR. These patients are included in the study cohort, but are recorded to be ineligible for EVAR on anatomic grounds.

Guidelines for Emergency AAA Stentgraft Procedures

The resuscitation of a patient with a ruptured AAA requires a multidisciplinary approach. It involves emergency, radiology, anaesthesiology, operating theatre and surgical staff. We prefer to maintain systolic blood pressure between 60 and 100 mmHg and avoid general anaesthesia. Emergency CT imaging should be available at

all times. The responsible surgeon confirms the diagnosis of rAAA (extravasation of blood), verifies the length and diameter of the neck and then decides whether EVAR or open surgery is the appropriate treatment.

Severe hypotension (less than 60 mmHg) can be treated by blood and crystalloid transfusion. Pain and anxiety can be treated by intravenous Fentanyl administering. If the blood pressure is > 100 mmHg systolic, Nitroproside or Ketansin is administered intravenously to lower the blood pressure. As soon as the decision is taken whether EVAR is possible the patient is quickly transported to the operating room for surgery.

The Talent aorto-uni-iliac stentgraft is favoured over a bi-iliac stent graft because it is presumed to be the quickest way to exclude an aneurysm from the systemic circulation.[19] An additional advantage of using an aorto-uni-iliac (AUI) device of one single company is that no subgroups need to be formed in the analysis and therefore the study does not lose power.

Emergency EVAR starts with local anaesthesia of the groin at the selected access side. After introduction of an angiography catheter, the renal arteries are marked on the fluoroscopy-display and the proximal part of the standard aorto-uni-iliac set is deployed. Then quickly the distal component of the stentgraft to the selected iliac artery is deployed. Sealing within the common iliac arteries is preferred over extending the device into the external iliac artery. Colon ischemia from hypogastric artery inflow occlusion is a real risk.

The contralateral common femoral artery is now exposed under local anaesthesia, and this artery is used for introduction of the 'Occluder device' (Figure 1) into the common iliac artery (if this artery is markedly aneurysmal the contralateral external iliac artery and hypogastric arteries are ligated via a small lower quadrant incision with retroperitoneal approach). The operation is finalised by performing a cross-over femorofemoral bypass under general anaesthesia. A completion angiogram is performed to check whether there are gross endoleaks.

Type I and III endoleaks have to be treated as soon as possible. Therefore they will be treated direct after the 'completion angiogram' in the same session, modifications are to the discretion of the participating physicians. Type II and IV endoleaks are accepted. Type II endoleaks are treated if there is growth of the aneurysm at follow-up. If Type IV endoleaks do not resolve in 30 days there should be concern that there is another type of endoleak present. All patients are postoperatively treated in the Intensive Care Unit.

Although the procedure described above is feasible, modifications are to the discretion of the participating physicians. Expedient preoperative CT-examination is strongly recommended, and it should be performed in the large majority of patients. However, in the case of extreme haemodynamic instability (systolic blood pressure < 60 mmHg or severe cardiac arhythmia) surgeons may decide to transport a patient immediately to the operating room. Depending on the circumstances one may choose to perform an angiogram using a C-arm fluoroscopy to determine whether EVAR is a reasonable option or to proceed with open surgery without imaging.

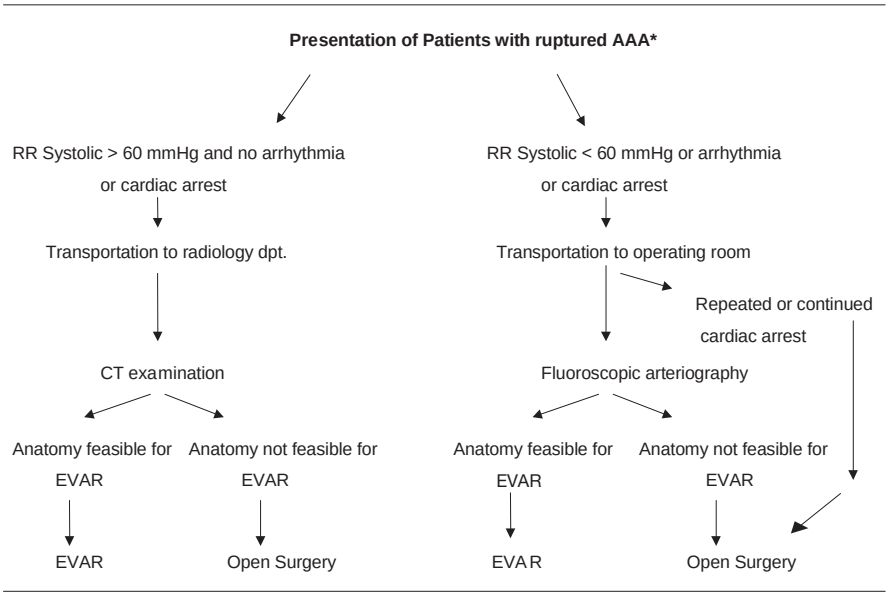

Figure 2: Flow sheet for patients with ruptured abdominal aneurysms entering the hospital. * patients who after treatment appeared to have a symptomatic aneurysm can not be included in the New Era-study.

Follow-up and Adverse Events

Clinical and imaging follow-up will be performed at 3 months after the intervention. Adverse events are documented, CT imaging results and secondary procedures are recorded.

Study Population and Statistical Analysis

Applicability

The applicability of the endovascular technique would be considered unsatisfactory if it were below 50%. Thus, the null hypothesis: applicability =50% will be tested against the one-sided alternative of a higher applicability rate. The expected applicability rate is at least 70%. With alpha set to 0.1 and a sample size of 100 patients the power would be 93%.

Mortality

The intention is to demonstrate that the mortality rate of patients with rAAA, treated by preferential EVAR, is lower than 50%. The null hypothesis of a first-month mortality of

50% or greater will be tested against the one-sided alternative of a lower mortality, using the exact binomial test. If a mortality rate of 25% is assumed in the group of patients treated by endovascular technique, and of 50% in the open surgery group, the overall mortality adds up to 32.5%, if the applicability of the endovascular technique is 70%. Under these assumptions and an alpha of 0.1 a sample size of 100 results in a power of 87% to reject the null hypothesis.

Secondary analysis

Preferential treatment will be EVAR, and open surgery will be performed only if patients do not meet the anatomical criteria for EVAR, or if the patient is in profound hypovolemic shock that does not allow CT-scanning or the use of IVUS during the operative procedure. A comparative, secondary, descriptive analysis between patients of the study group (patients undergoing endoluminal treatment and patients undergoing open surgery) and a historical patient group, with morbidity and mortality rates derived from literature, will be performed.

All case report forms, patient informed consents, data on adverse events will be reported by the investigator and monitored by Medtronic®. An Adverse Event Advisory Committee (AEAC) will review all severe or serious adverse events, device- or procedure-related, including death. Device-related and SAEs will be reported to all investigators. Each clinical participating site has obtained approval of the local ethical committee for the protocol. Data handling and analysis will be performed by the Department of Medtronic Clinical Research in co-operation with the chief clinical investigator.

Current Status

Recruitment began February 2003, and by the end of January 2004 a total of 59 patients have been included, representing 59% of the target. Final results of ERA should be available in 2005.

Conclusion

In this new era of endoluminal treatment, stentgrafting for ruptured infrarenal aneurysms has been reported in several non-consecutive, non-randomised trials with fair to good results. However, these results may be due to selection bias. The New ERA study is designed to diminish selection bias and optimise the applicability of EVAR. In the study, an international multicenter cohort of patients with rAAA will be treated preferentially by eEVAR, and the outcome of this group compared with that of patients with rAAA treated by conventional open surgery as reported in large series in the literature. If the results are again as promising as the first reports of treatment of

rAAA with stentgrafting, this study may pave the way to a randomised comparative trial for patients with rAAA.

About the ERA Study

The study is sponsored and supported by Medtronic® Bakken Research Center.
The Adverse Event Advisory Committee and the Steering Committee consists of members who are affiliated to Medtronic® and members who are not affiliated to Medtronic®. Statistical analysis will be performed by Medtronic Biostatistics and Data Management Department, Santa Rosa (CA).

Appendix Participants of the ERA-Study

J. Buth (principal investigator), P. Cuypers and N. Peppelenbosch, Eindhoven, J. Teijink, H. Odink and R. Welten, C.X. Heerlen, R.H. Geelkerken, A.B. Huisman, D.G. Gerrits, E.D.P. Volker, R. van Det and P. De Smit, Enschede, The Netherlands, J. De Letter, Brugge, F. E.G. Vermassen, and I. van Herzeele, Gent, Belgium, P. Cao, F. Verzini, and S. Mosca, Perugia, Italy, M.M. Thompson, R. Morgan, and A. Belli, London, United Kingdom, C. Soong, C. Boyd, and W. Loan, Belfast, Northern Ireland, M. Lepäntalo, P. Keto, W. Roth, and Pekka Aho, Helsinki, Finland, G. Walterbusch, N. Keck, and J. Beyer, Dortmund, Germany, G. DeRose, T.L. Forbes, and S.W. Kribs, London, Ontario, O. K. Steinmetz, K. MacKenzie, D. Obrand, and B. Montreuil, Montreal, Quebec, Canada.

Appendix Adverse Event Advisory Committee

B. Barbieri, and S. Zannetti, Medtronic® Bakken Research Center, Maastricht, J. v d Berg, Nieuwegein, The Netherlands, P. Cao, Perugia, Italy.

Appendix Steering Committee Members
B. Barbieri and S. Zannetti, Medtronic® Bakken Research Center, Maastricht, J.J. Jakimovicz, J. Buth, P. Cuypers and N. Peppelenbosch, Eindhoven, The Netherlands.

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CHAPTER VII

Endograft treatment of ruptured abdominal aortic aneurysms using the Talent® aorto-uni-iliac system: An international multicenter study

N. Peppelenbosch, R.H. Geelkerken, C Soong, P. Cao, O.K. Steinmetz, J.A.W. Teijink, M. Lepäntalo, J. De Letter, F.E.G. Vermassen, G. DeRose, E. Buskens, J. Buth

J Vasc Surg 2006; 43:1111-1122

Abstract

Objective: To understand the potential of endovascular aneurysm repair (EVAR) in patients presenting with a ruptured abdominal aortic aneurysm (rAAA), the proportion in whom this procedure was applicable was assessed. Mortality and morbidity was also determined in patients treated with emergency EVAR (eEVAR) when anatomic and hemodynamic conditions allowed (i.e., in the entire cohort with patients receiving endovascular and open repair combined). In addition, a comparison was made between the treatment group with eEVAR and open repair.

Methods: Between February 2003 and September 2004, 10 participating institutions enrolled a representative sample of 100 consecutive patients in whom eEVAR was considered. Patients in the New Endograft treatment in Ruptured abdominal aortic Aneurysm (ERA) trial were offered eEVAR or open repair in accordance with their clinical condition or anatomic configuration. Written informed consent was obtained from all patients or their legal representatives. The study included patients who were treated by stentgraft technique or by open surgery in the case of adverse anatomy for endoluminal stentgrafting or severe hemodynamic instability, or both. Data were collated in a centralised database for analysis. The study was sponsored and supported by Medtronic, and eEVAR was uniquely performed with a Talent® aorto-uni-iliac (AUI) system in all patients. Crude and adjusted 30-day or in-hospital and 3-month mortality rates were assessed for the entire group as a whole and the EVAR and open repair category separately. Complication rates were also assessed.

Results: Stentgraft repair was performed in 49 patients and open surgery in 51. No significant differences were observed between these treatment groups with regard to comorbidity at presentation, hemodynamic instability, and the proportion of patients who could be assessed by preoperative computed tomography scanning. Patients with eEVAR more frequently demonstrated a suitable infrarenal neck for endovascular repair, a longer infrarenal neck, and suitable iliac arteries for access than patients with open repair. The primary reason to perform open aneurysm repair was an unfavourable configuration of the neck in 80% of the patients. In patients undergoing eEVAR, operative blood loss was less, intensive care admission time was shorter, and the duration of mechanical ventilation was shorter ($P \leq .02$, all comparisons). The 30-day or in-hospital mortality was 35% in the eEVAR category, 39% in patients with open repair, and 37% overall. There was no statistically significant difference between the treatment groups with regard to crude mortality rates or rates adjusted for age, gender, hemodynamic shock, and pre-existent pulmonary disease. The cumulative 3-month all-cause mortality was 40% in the eEVAR group and 42% in the open repair group (no significant differences at crude and adjusted comparisons). The 3-month primary complication rate in the two treatment groups was similar at 59%.

Conclusions: In approximately half the rAAA patients, eEVAR appeared viable. An unsuitable infrarenal neck was the most frequent cause to select open repair. In dedicated centers using a Talent® AUI system, eEVAR appeared to be a feasible method for treatment of a rAAA. The overall first-month mortality did not differ across treatment groups (patients with endovascular and open repair combined), yet was somewhat lower than observed in a recent meta-analysis reporting on open repair.

Introduction

Abdominal aortic aneurysms (AAAs) >5.5 cm in diameter have a significant risk of rupture, which again increases substantially when the aneurysm diameter is >6.5 cm.[1,2] Furthermore, open surgical repair of ruptured AAA (rAAAs) has typically been associated with an average in-hospital mortality of 50%[3-7] and only a modest improvement in the outcome of rAAA repair was documented in a recent meta-analysis in which the average mortality rate achieved in the year 2000 was estimated at 41%.[8] Endovascular abdominal aortic aneurysm repair (EVAR) of elective patients has been demonstrated to be associated with lower 30-day mortality and morbidity rates than open repair.[9,10] Meanwhile, the use of emergency EVAR (eEVAR), as assessed in a number of studies,[11-25] has been associated with a mean first-month mortality rate of 18.4% (range, 0% to 45%). The improved outcomes in these reports may reflect selective patient recruitment, however, with patients selected for eEVAR constituting a lower-risk category because they would need to be stable for preoperative imaging and have a suitable anatomic configuration for EVAR. Thus, the favourable outcomes observed in the previous studies may simply reflect selection bias.

Several questions regarding the use of eEVAR in rAAAs remain. Among these uncertainties, the applicability rate for eEVAR is a key factor. In particular, the anatomy of the infrarenal neck and the patency of the iliac arteries may preclude successful endovascular repair. Additionally, primary outcome events that need to be addressed include the mortality rate of eEVAR in all patients who are candidates for endovascular treatment and the effect of a preferential eEVAR policy on mortality in an unselected group of patients with rAAA. Furthermore, the infrastructural requirements, such as the availability of rapid preoperative imaging and around the clock surgeons experienced in emergency endovascular aneurysm repair, need to be assessed.

The present observational study, which is designated the New ERA (Endograft treatment in Ruptured abdominal aortic Aneurysm) trial, was designed to overcome selection bias for an optimal assessment of eEVAR in the treatment of rAAA. This report describes an international multicenter cohort study of patients with rAAA who were treated preferentially by eEVAR using a Talent® aorto-uni-iliac (AUI) stentgraft (Medtronic, Santa Rosa, Calif). The outcome in the entire study group was assessed to allow a comparison with mortality rates in patients treated by conventional open surgery as reported in the literature. Additionally, the results observed in the eEVAR group were compared with those in the open repair group.

Methods

The New ERA study is a prospective, multicenter European and Canadian study that is sponsored and supported by Medtronic and the Bakken Research Centre (Maastricht, the Netherlands). Ten centers participated in the study. Each participating clinical site had obtained approval of the protocol from the local ethics committee.

Vascular surgeons and interventional radiologists with considerable experience in the diagnosis and open and endo-vascular treatment of rAAA were included as investigators in this study. A list of participating investigators is in the Appendix. Patient data and procedural details were recorded in a structured case report form (CRF) and periodically monitored on-site by representatives of the organizing company. All adverse events, including device-and procedure-related events, and death were reviewed by an independent Adverse Event Advisory Committee. Study conduct was supervised by a Steering Committee. The first author and the principal investigator had access to all CRFs at the end of the study period. The evaluation of the study objective required 100 patients, each with a follow-up of 3 months. Enrollment into the study started in February 2003 and ended in September 2004.

The protocol specified that in each of the participating centers, a consecutive series of patients treated for ruptured infrarenal AAAs, who had given their informed consent, were expected to be included in the study. The preferential treatment was EVAR. The protocol recommended that open surgery was only to be selected as the treatment when anatomic criteria precluded effective exclusion of the aneurysm or if the patient was in profound hypovolemic shock (see the definition of severe hemodynamic instability below) that did not allow a preoperative computed tomography (CT) examination, fluoroscopy, or the use of intravascular ultrasound (in one of the institutions) to evaluate feasibility for EVAR. In other words, included in the study were patients treated by stentgraft technique or by open surgery in the case of adverse anatomy for endoluminal stentgrafting or severe hemodynamic instability.

Patients who were suitable for EVAR were treated with a uniform technique and a single endovascular device, the Talent® AUI stentgraft system (Figure 1) combined with a femoro-femoral bypass. The number and outcome of the treatment of patients who did not give their informed consent or were otherwise not enrolled, for example, because the surgeon did not ask them to participate, and the reasons for exclusion, were obtained from each of the participating institutions by a questionnaire at the end of the study.

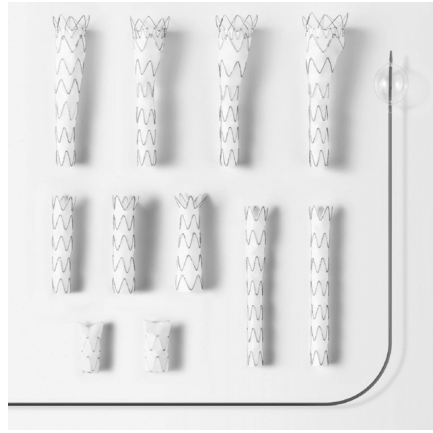

Figure 1. The components of the Talent® aorto-uni-iliac stentgraft system used for emergency EVAR

Purpose and objectives

The New ERA study had three main purposes. The first was to assess the proportion of patients presenting with rAAA in whom EVAR by the Talent® AUI device could be used. The second was to determine the operative mortality and morbidity in a cohort of patients treated with eEVAR when possible, according to present anatomic and hemodynamic criteria. This analysis comprised the entire study group with patients

who underwent endovascular or open surgery. Finally, the mortality and morbidity in the eEVAR and open repair groups was compared. Study end points included operative mortality, defined as death ≤ 30 days or during the same hospitalization, and major morbidity, defined as serious adverse events. Secondary end points included death from all causes and major morbidity ≤ 3 months after the procedure.

Patient selection, inclusion, exclusion criteria, and management

Details of the inclusion and exclusion criteria, management of the patient, and the technical execution of the eEVAR by implanting the Talent® AUI device were described previously in an article on the design and planning of this study.[26] Each participating center was expected to enroll its series of patients with rAAA that met the inclusion criteria consecutively throughout the study period.

Briefly, the protocol required that on arrival in the emergency department, intravenous fluid infusion was minimised, and if necessary, medication to lower blood pressure was administered. If the hemodynamic situation allowed an emergency CT examination, this was performed.

Aneurysm rupture was defined as hemorrhage outside the aortic wall or by direct observation in case of laparotomy. By protocol, when there was still doubt after treatment whether the aneurysm was ruptured, extravasation was to be confirmed by postoperative CT examination or by autopsy. The patient or his or her relatives were informed about the study and asked permission to participate by a written informed consent. The main exclusion criteria for enrollment in the study were not consenting to participate and comorbidities with a life expectancy of < 1 year. Thus, the study group consisted only of patients who met the inclusion criteria and had signed (or their relatives or legal representative) the informed consent.

An urgent CT examination was done in patients in stable hemodynamic condition or with *moderate hemodynamic instability*, referred to in this analysis when the patient had a systolic blood pressure between 60 and 100 mm Hg, was conscious, and had no episodes of cardiac arrest. The selection of patients for CT examination and subsequently for EVAR or open repair was according to the algorithm represented in Figure 2. This flow sheet dictated the decisions to be taken at initial management, although it was left to the discretion of the participating surgeon to deviate from these suggested guidelines. The algorithm advised that *severely hemodynamically unstable* patients with a systolic blood pressure of < 60 mm Hg, decreased consciousness, or with episodes of cardiac arrest, should be taken to the operating room and, if possible, undergo fluoroscopic assessment to establish whether an EVAR or open surgical procedure should be performed. The use of intra-aortic balloon inflation to increase a low blood pressure was again left to the discretion of the attending surgeon.

The suggested anatomic criteria for treatment by open surgery included an infrarenal aortic neck of < 10 mm or a diameter of > 32 mm, or both. In addition, an angulation of the infrarenal neck of > 85° was considered an exclusion criterion for EVAR, as were bilateral iliac artery occlusions or stenosis (< 6 mm diameter) not amenable to balloon angioplasty.

After CT examination, patients were quickly transported to the operating room for the selected emergency procedure. In endovascularly treated patients, the preferred operative technique in rAAA was an AUI stentgraft implantation. The reasons for this preference, which is shared with several other groups, include a larger application rate of the stentgraft technique because of less anatomic restrictions and a quicker decompression of the bleeding aneurysm.[14,16,21,22] AUI endografting was combined with a crossover bypass and the deployment of an Occluder cuff in the contralateral iliac artery. The standard emergency set of AUI stentgrafts and distal extender iliac device limbs (Talent® , Medtronic, Santa Rosa, CA) represented in Figure 1 was permanently available in the ten centers.

It was recommended that eEVAR be commenced under local anesthesia of the groin at the selected access site. The rational for using local anesthesia in the initial part of the procedure has been described previously by our group and by others.[26,27] The general idea is to avoid a severe circulatory collapse associated with the induction of general anesthesia in the patient with extensive retroperitoneal blood loss because of vasomotor relaxation.[28] In addition, the loss of abdominal tone, which increases the risk of a contained rupture becoming an intra-abdominal hemorrhage, is minimised by the use of local anesthesia.

After the AUI device was inserted and the antegrade flow into the ruptured aneurysmal sac was blocked, general anesthesia could be given to perform the subsequent operative steps, which consisted of exploration of the contralateral common femoral artery, deployment of the common iliac Occluder cuff at this side, and performing the cross-over femorofemoral bypass. Also with regard to the technical execution of the procedure, the managing team could deviate from any of the suggested steps except implantation of the Talent® AUI device when the patient was treated by endovascular technique.

Statistical analysis

A priori, the applicability of the endovascular technique was considered unsatisfactory if it would be < 50% of the patients. The intention was to demonstrate that the mortality rate of consecutively enrolled patients with rAAA, treated by preferential EVAR, would be < 50%. As for secondary study end points, a comparative analysis between the eEVAR and open repair groups was powered to demonstrate a statistically significant 30-day or in-hospital mortality of ≤ 25% in the patients that had received eEVAR compared with 50% in the open repair group.

Crude and adjusted hazard ratios with the 95% confidence intervals (CI) and P values were assessed for differences in mortality rates in the subgroups. The factors for which adjustment was made included advanced age, male gender, hemodynamic shock (systolic tension ≤ 100 mm Hg), and a history of pulmonary disease. These factors were previously observed to influence outcome in patients undergoing rAAA repair.[3,5]

The data processing and analysis were performed by the first author and the principal investigator, with the technical assistance of Medtronic. A statistician (E. B.) reviewed

the manuscript and the validity of the conclusions. Results were reported as means, standard deviation, or ranges. Differences in findings between treatment groups were assessed by χ^2 or Fisher exact tests for discrete variables and by Mann-Whitney tests for continuous variables. Selected variables were entered in a multivariate regression analysis, and a Cox analysis was used to assess independent associations with the 3-month mortality rate. Only moderate or severe adverse postoperative events [29,30] were taken into account. Per patient, the initial or most severe complication, or both, was considered for the analysis. All analyses were performed by SAS 9.1 statistical software (SAS Institute, Inc, Cary, NC).

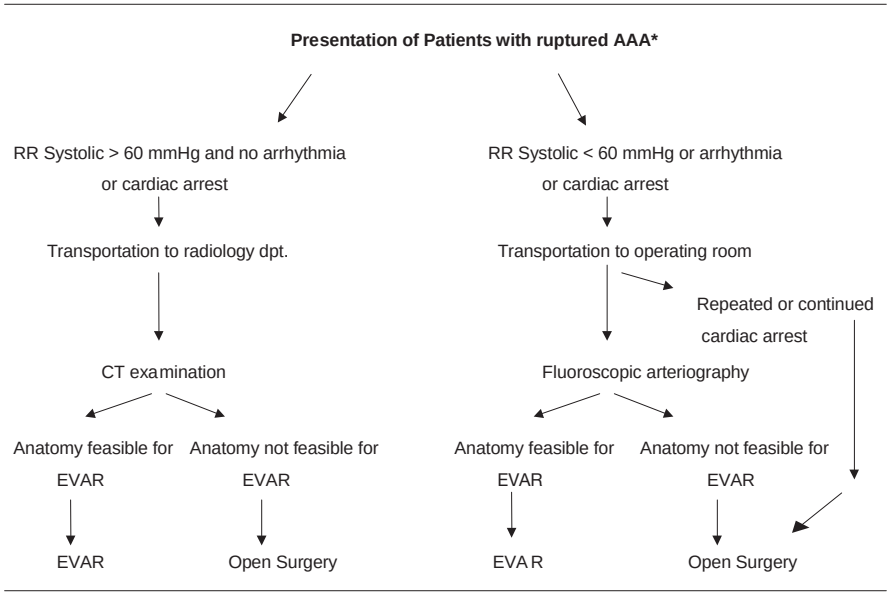

Figure 2: Flow sheet for patients with ruptured abdominal aneurysms (AAA) entering the hospital. In patients with stable hemodynamic condition (systolic BP > 100 mmHg) and with moderate hemodynamic instability (systolic BP 60 - 100 mmHg without cardiac arrhythmia) preoperative CT-examination was to be performed. Patients with severe hemodynamic instability (systolic BP < 60 mmHg, with arrhythmia) were immediately taken to the operating room. * Patients who after treatment appeared to have a symptomatic aneurysm can not be included in the New Era-study

Results

Between February 2003 and September 2004, 100 patients (83 men and 17 women) with a mean age of 74 years (range, 58 to 90) were enrolled in the study. The number of study patients from different centers varied between 2 and 23 (mean, 10 patients). Forty-nine patients underwent eEVAR, and 51 had operative repair. Table I summarizes the baseline characteristics of the patients in the two treatment groups.

Hemodynamic instability at presentation was observed in 43 patients (43%), and the mean systolic blood pressure was 100 mm Hg (range, 0 to 200 mm Hg). There were no differences between the treatment groups with regard to any of the assessed preoperative variables, including the presence and severity of hemodynamic instability.

Preoperative use of an occluding aortic balloon to prevent severe hemodynamic collapse was needed in seven patients: three in the eEVAR group and four in the open repair group. The median time from admission to the procedure was 90 minutes (range, 10 to 3060) for the endovascular group and 60 minutes (range, 12 to 1440) for the open repair group; this difference was not statistically significant. Preoperative CT examination was performed in 87 patients (87%) (Table II). In seven patients (7%), an ultrasound examination revealed a rAAA, but the patients were severely hemodynamically unstable and the surgeon elected not to perform CT scanning. These patients were directly transported to the operating room, where six underwent open repair and the seventh underwent fluoroscopic assessment followed by endovascular repair. In five patients (5%), all in one institution, intravascular ultrasonography (IVUS) was performed. In this center, it was the policy that IVUS was used instead of preoperative CT examination. One patient (1%) was reported to have had a magnetic resonance angiography to assess the vascular anatomy.

Forty-nine patients had a suitable anatomy and were treated with eEVAR (Table III) for an overall applicability rate for eEVAR of 49%. Three additional patients, according to their CT findings in retrospect, appeared suitable for eEVAR. At the time of admission, however, unavailability of experienced endovascular staff (in two) or severe hemodynamic instability (in one) precluded eEVAR. Taking these cases into account, at least 52% of the study cohort had a vascular morphology that would have allowed an EVAR procedure.

The principal reason to perform an open aneurysm repair was an adverse configuration of the neck in 40 patients: the neck was too short in 34 patients, too angulated in two, and the diameter too wide for available devices in four. It should be noted that accepted criteria for neck length in EVAR were not followed rigorously, as endovascular repair was performed in five patients with a neck < 10 mm. Other adverse anatomic factors included small diameter or occluded iliac arteries in two patients and iliac arteries that were too angulated in 14 patients. Moreover, moderate or severe hemodynamic instability precluded EVAR in seven patients (14%).

At statistical comparison, a number of anatomic characteristics were different in the treatment groups. Patients with eEVAR more frequently demonstrated an infrarenal neck suitable for EVAR and longer necks (Table III). No significant differences were observed in aneurysm diameter, neck diameter, angulation of the neck, iliac arteries suitable for EVAR, and angulation of iliac arteries. This comparison did not include patients with open repair who were not examined by CT because of severe hemodynamic instability.

Table I. Baseline characteristics of patients presenting with rAAA treated by eEVAR or open repair

	eEVAR (n=49)	Open repair (n=51)	All patients (n = 100)
Demographic details			
Male/female	42/7	41/10	83/17
Age ± SD (years)	75.1 ± 7.1	73.8 ± 7.9	74.4 ± 7.5
History (% of group)			
Cardiac	9 (18%)	8 (16%)	17 (17%)
Pulmonary	14 (29%)	13 (25%)	27 (27%)
Renal	7 (14%)	11 (22%)	18 (18%)
Carotid	4 (9%)	12 (24%)	16 (16%)
Details at admission			
Abdominal pain	45 (92%)	45(88%)	90 (90%)
Collapse of patients	27 (55%)	26(51%)	53 (53%)
Hemodynamic instability	21 (43%)	22 (43%)	43 (43%)
Moderate*	16 (33%)	19 (37%)	35 (35%)
Severe **	5 (10%)	3 (6%)	8 (8%)
Lowest systolic BP mean ± SD (in mmHg)	100 ± 41	101 ± 42	101 ± 42

Figures indicate number of patients unless indicated otherwise.
* systolic blood pr essure 60 - 100 mmHg
** systolic blood pressure < 60 mmHg

Table II. Preoperative imaging

	eEVAR (n=49)	Open repair (n=51)	All patients (n = 100)
Ultrasound (US)	1 (2%)*	6 (12%)	7 (7%)
CT-scanning (with or without US)	43 (88%)	44 (86%)	87 (87%)
IVUS	5 (10%)	-	5 (5%)
MRA	-	1 (2%)	1 (1%)

US Ultrasound
CT Computed tomography
IVUS Intravascular ultrasound
MRA magnetic resonance angiography

*This patient who had a preoperative US study subsequently underwent intraoperatively fluoroscopy and endovascular repair.

The procedure and early course

The anesthetic technique involved general anesthesia in all patients with open repair compared with 33 patients with eEVAR (P<.05). In this latter category, 21 patients had local anesthesia during the initial part of the procedure and general anesthesia after deployment of the AUI device, whereas regional or local anesthesia exclusively was used in 16 eEVAR patients. Twelve patients had general anesthesia for the entire procedure. Procedural details for each of the two treatment modalities are shown in

Tables IV and V. Suprarenal control by clamping during the procedure in patients with open repair was significantly more frequent than suprarenal balloon occlusion in patients with eEVAR (P=.001). The volume of replaced blood was less in the eEVAR group (P=.001). A primary conversion to open repair was required in three eEVAR patients (6%) because of device migration that caused a persistent type III endoleak in two and because the device could not be advanced as a result of too narrow iliac arteries in one. The distal landing zone in the other 46 patients with endovascular repair was in the common iliac artery in 36 and in the external iliac artery in 10 patients. Endoleaks at completion angiography were identified and accepted in 11 patients (22%).

No group differences were observed with regard to the duration of the procedure; however, the intensive care unit stay was significantly shorter in the eEVAR group than in the open repair group (Tables IV and V). The same was true for time on the ventilator. There was no statistically significant difference in hospital stay between the groups.

Table III. Anatomical characteristics[1] in patients, who had preoperative imaging[2]

	eEVAR (n=49)	**Open repair (n=44)**	**All patients (n = 93)**
Aneurysmal neck suitable (%)*	49 (100%)*	11 (25%)*	60 (65%)
Proximal neck length, mean ± SD (mm)**	21 ± 12**	9 ± 12**	16 ± 13
Proximal neck diameter, mean ± SD (mm)	25 ± 3	25 ± 8	25 ± 6
Iliac arteries suitable (%)	47 (96%)	35 (80%)	82 (88%)
Aneurysm diameter, mean ± SD (mm)	75 ± 16	80 ± 15	78 ± 15

[1] more factors per patient were possible; [2] either CT examination, MRA, IVUS or US followed by fluoroscopy; * $p < 0.0001$; ** $p < 0.0001$.

Table IV. Operative details in patients with eEVAR

	eEVAR (n=49)
Use of supra-renal balloon	3 (6%)*
Deployment success	45 (92%)
Conversion to open repair	3 (6%)
Fluoroscopic time, mea n ± SD (min)	19 ± 9
Post-operative completion angiogram endoleak	11 (22%)
Type I prox.	*3*
Type I dist	*4*
Type II	*4*
Type III	-
Operation time, mean ± SD (min)	173 ± 60
Replaced blood volume, mean ± SD (ml)**	1322 ± 1494**
I.C.U. stay, mean ± SD (days)***	5.8 ± 9.4***
Mechanical ventilation, mean ± SD (hours)****	71 ± 159****
Hospital stay, mean ± SD (days)	14.9 ± 16.4

* $p < 0.001$ (compared wi th suprarenal clamping in open repair Table V)
** $p = 0.001$ (compared with open repair Table V)
*** $p = 0.019$ (compared with open repair Table V)
**** $p=0.001$ (compared with open repair Table V)

Table V. Operative details in patients with open repair

	Open repair (n=51)
Supra renal clamping	22 (43%)*
Aortic cross clamp time, mean ± SD (min)	56 ± 27
Tubegraft/bifurcated graft used	35/16
Operation time, mean ± SD (min)	177 ± 54
Replaced blood volume, mean ± SD (ml)**	2411 ± 2159**
I.C.U. stay, mean ± SD (days)***	9.4 ± 14.6***
Mechanical ventilation, mean ± SD (hours)****	165 ± 317****
Hospital stay, mean ± SD (days)	22.2 ± 28.2

* p = 0.001 (compared with eEVAR Table IV)
** p = 0.001 (compared with eEVAR Table IV)
*** p=0.019 (compared with eEVAR Table IV)
**** p=0.001(compared with open repair Table V)

Table VI. Mortality in patients with eEVAR and open repair

	eEVAR (N=49)	Open repair (N=51)	Odds ratio and Hazard ratio from multivariate regression models 95% CI, p -value	
				adjusted*
30-day or in-hospital mortality*	17 (35%)	20 (39%)	operation type age gender shock Hx pulmonary	1.14 (0.46 – 2.80; p = 0.78) 1.05 (0.98 – 1.12; p = 0.19) 1.91 (0.55 – 6.64; p = 0.31) 3.85 (1.57 – 9.47; p = 0.003) 1.41 (1.00 – 1.97; p = 0.05)
3-month all cause mortality*,**	20 (40%)	22 (42%)	operation type age gender shock Hx pulmonary	1.20 (0.65 – 2.24; p = 0.56) 1.02 (0.98 – 1.08; p = 0.35) 1.51 (0.66 – 3.46; p = 0.33) 2.69 (1.52 – 5.58; p = 0.0013) 2.22 (1.19 – 4.14; p = 0.0121)

* adjusted for: operation type, age, gender, shock (systolic BP ≤ 90mmHg) and pulmonary history.
** adjusted for follow -up time (see Figure 3)

Mortality

The overall 30-day or in-hospital mortality was 37 (37%) for the entire study group; 17 (35%) died in the eEVAR group and 20 (39%) in the open repair group. There was no statistically significant difference between the type of operation and crude or adjusted mortality rates (Table VI).

The all-cause mortality at 3 months was 40% in patients with eEVAR and 42% in the open repair category (difference not statistically significant) (Figure 3). The adjusted 3-month mortality was not different for the treatment groups (Table VI). Independent asso-

ciations were found between hemodynamic shock at admission (systolic blood pressure < 90 mm Hg) and a history of pulmonary disease and mortality. The causes of death are listed in Table VII and included hemorrhage, cardiac arrest, respiratory insufficiency, and multiorgan failure as the most frequent causes of death. No statistically significant differences were found between the participating centers and the overall mortality.

Table VII. Causes of death

	eEVAR (n=49)	Open repair (n=51)	all patients (n = 100)
30 Day or in-hospital total	***17 (35%)***	***20 (39%)***	***37 (37%)***
Hemorrhage	6	6	12
Cardiac	3	3	6
Pulmonary	3	4	7
Bowel	2	2	4
M.O.F.*	3	4	7
Miscellaneous	-	1	1
1-3 Month total	***3 (6%)***	***2 (4%)***	***5 (5%)***
Cardiac	-	1	1
Pulmonary	1	1	2
M.O.F.*	1	-	1
Miscellaneous	1	-	1

* Multi organ failure (failure of ≥ three organs)

Table VIII. Primary complications

	30 Day or in-hospital*		1-3 Month period**	
	eEVAR (n=41)	Open repair (n=44)	eEVAR (N=29)	Open repair (N=29)
Cardiac	5 (12%)	5 (11%)	-	1 (4%)
Pulmonary	2 (5%)	4 (9%)	-	-
Renal (with dialysis)	1 (2%)	1 (2%)	-	-
Bowel ischemia	2 (5%)	3 (7%)	-	-
Paraplegia	2 (5%)	2 (5%)	-	-
Re-intervention - total	3 (7%)	3 (7%)	1 (4%)	-
Thrombectomy	*1*	*2*	-	-
Ffx infection¶	-	-	*1*	-
Late conversion	*1*	-	-	-
Laparotomy	*1*	*1*	-	-
Multi organ failure ?	5 (12%)	5 (11%)	1 (4%)	-
Miscellaneous	-	-	2 (7%)	2 (7%)
TOTAL	**20**	**23**	**4**	**3**

Ffx: femorofemoral prosthesis. Figures indicates number of patients unless indicated othe rwise; Patients are categorized to their most severe complication. ¶ femorofemoral crossover bypass replaced by vein ; ? failure of ≥ three organs; * of 24 hour survivors ; ** of 30 Day or in-hospital survivors

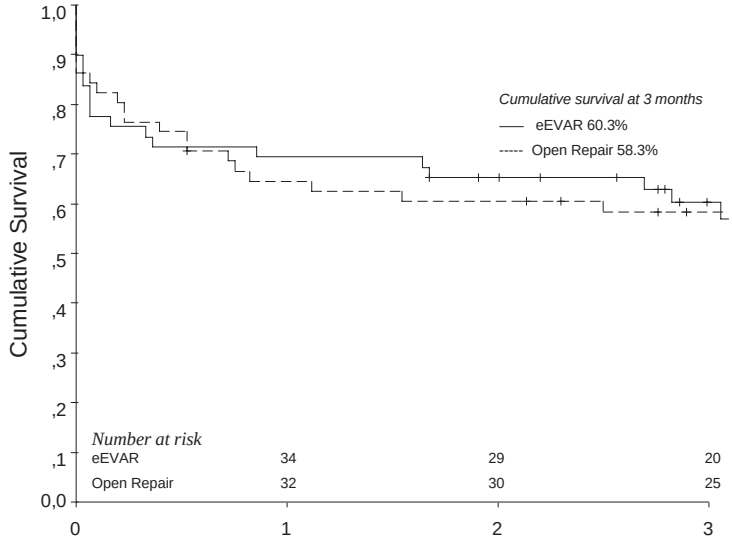

Figure 3. Kaplan Meier Survival curve for eEVAR patients and open repair patients

Complications

The primary postoperative complications in 24-hour survivors and reinterventions that occurred ≤ 30 days and from 1 to 3 months are summarised in Table VIII. There was no difference with regard to the overall number of complications or the different types of complications between the treatment groups. Of the 85 24-hour survivors, 50 patients (59%) experienced one or more complications: 24 patients (59%) in the eEVAR group and 26 patients (59%) in the open repair group. Reinterventions by laparotomy in the eEVAR group included a banding at the infrarenal neck 4 days post-operatively for a type I endoleak that had caused a secondary rupture. In another patient, a secondary conversion to open repair was performed because of a type I proximal endoleak. Notably, paraplegia developed in four patients (4%), two in each treatment group.

Excluded patients

During the study period, 134 patients were not enrolled in the study (data obtained by questionnaire). The number of patients excluded from each participating center ranged from 2 to 39, and the proportion of excluded patients ranged from 12% to 94%. Four centers were responsible for 113 (84%) of all patients not enrolled. The reasons that patients were not enrolled included informed consent not obtained or asked for,

endovascular team unavailable, suprarenal aneurysm (which was in fact an exclusion criteria for this study), severe hemodynamic instability (which condition would have allowed inclusion with the option of allocating the patient to immediate open repair), and the use of a bifurcated stentgraft system of a different brand (one patient). Frequently, more than one reason was reported. The mean perioperative mortality in the patients excluded was 41%.

Discussion

Although an immense increase in the expertise with EVAR in elective cases was observed during the last decade, only a limited number of centers have thus far published their experience with EVAR in rAAAs.[11-27] The present study was organised in cooperation with Medtronic. It was intended to systematically assess the outcome of treatment in a consecutive patient cohort undergoing either endovascular or open repair. This design, which differed from previous studies on emergency use of EVAR, was chosen to evaluate the following aspects: the applicability rate or the proportion of patients with anatomy that would allow endovascular repair, the overall perioperative mortality rate, and the mortality and morbidity rates in the endovascular and open repair groups separately. The study was organised as multicenter project to assess emergency rAAA repair using endovascular techniques where applicable. A broad range of institutions participated to accumulate a sufficiently large cohort in a short period, to realistically reflect current practice, and to allow for generalization of our findings. The study was set up as a feasibility study, and a number of notable findings evolved from this effort.

The proportion of patients with anatomic dimensions allowing endovascular repair reported in previous reports varied from 28% to 83%.[15,17,21,24,25] In the present study group, half of the patients underwent eEVAR. Adverse anatomy appeared to be the most frequent reason for selecting open repair. Logistic factors such as unavailable endovascular expertise precluded eEVAR in the study group in only 6% (three patients) of the open repair group. The potential effects of the relatively large number of excluded patients (often also because of logistic factors) will be considered at the end of this discussion.

Lower eligibility rates (23% to 37%) indicated in a number of previous reports[15,17,20-22] were probably associated with more restrictive anatomic criteria than recommended in our study protocol.[26] Five patients in the EVAR group (10%) had necks of < 10 mm (our recommended threshold), and another 11 patients (22%) had necks of < 15 mm (often suggested as a contraindication for elective EVAR). These observations signify that the anatomic criteria for eEVAR were applied liberally in the present study. Rigid application of generally recommended anatomic guidelines, well justified in elective EVAR, seems counter-productive in emergency treatment of rAAA. However, the safety and efficacy of the expanded criteria remain to be determined even though our outcomes appear generally favourable.

A preoperative CT examination was performed in 87% of the patients in an almost equal proportion of the two treatment groups. Hemodynamic status (i.e., severe or moderate instability on average) was comparable in the two treatment groups; however, hemodynamic instability precluded any other imaging than ultrasound scans in 12% in the open repair group. In retrospect, our categorization into moderate and severe hemodynamic instability, meant to assist in decision-making, did not correlate with the selected treatment. Apparently, the response to hemodynamic shock varies from one surgeon to another. Some will prefer open repair in a critical situation, whereas others will proceed with EVAR if the arterial morphology allows. In the eEVAR-group, 10% underwent preoperative IVUS (all in one center) instead of CT examination. In only one patient, the alternative pathway of triage between eEVAR or open repair by fluoroscopic arteriography immediately before the intervention was used. Thus, a CT examination is possible in almost all patients with rAAA. This is in agreement with the findings of Lloyd et al,[31] who observed that of patients who did not undergo repair of their aneurysm, 87.5% survived for more than 2 hours after admission in hospital.

The Talent® AUI stentgraft was adopted as the single endovascular device in this study to reduce a large variation in operative technique and device characteristics. The use of an AUI stentgraft reduces intra-aneurysm sac pressure more effectively than bifurcated devices, as was confirmed in model study by Gawenda et al.[32] This advantage is greatest in unstable patients. Moreover, in patients with elective EVAR, AUI devices increased the proportion of patients treatable by endovascular technique by 19% to 45% because an unilateral access problem did not preclude the endovascular repair.[33,34] This aspect applies also to ruptured aneurysms. An additional advantage is the shorter learning curve with AUI stentgrafts compared with bifurcated stentgrafts, which may increase the number of centers that can perform eEVAR in rAAA.[35]

The use of a femorofemoral prosthetic bypass is considered a disadvantage by some. Potential risks include late occlusion or infection of the prosthetic bypass.[36] In the present study, only one patient had a prosthetic infection, which was successfully treated by replacing the crossover bypass by a vein graft. In an overview of the literature, it was concluded that the complication rate of femorofemoral bypasses in combination with AUI devices was low, and the long-term patency was excellent.[36-38]

Of 24-hours survivors, 59% had moderate or severe postoperative complication (Table VIII). Others have reported a comparable high figure,[23] but in other series this rate was lower (22% to 46%).[14,16,17,24] A likely explanation for the higher major morbidity is that the present study was prospective, which usually accounts for a higher reported rate of complications. Similar to most reports on open and endovascular repair, multiorgan failure, limb ischemia requiring thrombectomy, and cardiac and respiratory events were frequent complications in both treatment groups. Although we anticipated that eEVAR might be associated with fewer complications than open repair, the incidences in both groups were similar. The 4% rate of paraplegia was surprising. An assessment of the pathogenesis and risk factors of this complication after eEVAR was recently published by some of the present authors.[39]

The 30-day mortality in the present trial was considerably higher compared with some published single institution series in which this rate in eEVAR patients was 8% to 14%.[18,22-24] There may be several explanations for this difference:

First, selection bias seems a reasonable explanation of the seemingly favourable results observed in previous studies. In particular, a small number of patients underwent endovascular treatment, and the outcome in patients with open surgery for their ruptured aneurysms in the same period was not reported.

Second, the presence of severe or multiple comorbidities may cause different outcomes between series. Notably, medical eligibility for open repair was not a prerequisite for enrolment in the present study, which may have resulted in the acceptance of patients with quite severe comorbidities for endovascular repair.

Third, hemodynamic status is strongly associated with the overall outcome. In a recent series by Hechelhammer et al,[24] only 22% of their patients were in hemodynamic shock preoperatively, as opposed to twice as many (43%) in the present study (systolic blood pressure of < 100 mm Hg in both studies).

The higher percentage of patients treated by endovascular repair in combination with less favourable prognostic factors (confounders), compared with most of the previously reported series, may very well explain the higher mortality in the present study. Nevertheless, the 35% mortality rate in the eEVAR group and the 37% mortality in the study group overall still compare favourably with the often observed 40% to 50% perioperative mortality in open repair series.

One may consider that essentially three types of patients with rAAA will present for treatment. The first category includes the patient who will not survive the first postoperative month irrespective of whether the operation is by endovascular or by open surgical technique. Death in this patient category appears unpredictable; no single preexisting risk factor can reliably indicate the expected clinical course, as was assessed in earlier open repair series.[3,5] Patients in the second category may be assumed to survive any type of repair. For these two categories, the introduction of EVAR will not be of decisive importance. At most, the duration of the intensive care unit admission or the number of days on the ventilator may be less with eEVAR. Finally, a third category may be recognised. This group consists of patients that will not tolerate the initial challenge of a laparotomy, aortic clamping, lower-limb ischemia, hypothermia, and systemic and coagulation disturbances. This may be the patient who survives the perioperative period because of the lesser challenge of the endovascular procedure. How large this proportion of patients is cannot be estimated at the present time.

The large number of patients who were excluded because no informed consent was obtained was disturbing and, at first sight, appears to undermine the validity of this study. In fact, 134 non-enrolled patients underwent open repair, except one in whom implantation of a bifurcated endograft from another company was performed. However, since informed consent was not obtained or asked for (largely because the attending surgeon was inexperienced in eEVAR) for most of the nonenrolled patients, selection leading to a bias is not an issue. Not asking for informed consent in an emergency situation or because personnel requirements were not met may be considered

a random phenomenon with regard to patients being admitted for rAAA, that is, it did not result in systematic inclusion of patients with exceptionally good or poor prognosis. In fact, this observation signifies the large organizational challenges even in dedicated centers with the endovascular management of emergency cases.

The proportion of nonenrolled patients with an unsuitable anatomy for EVAR could not be examined because CT examination was rarely performed. Still we have no reason to assume that the EVAR application rate is different from the group that was included. In particular, the first-month mortality was very much similar in patients enrolled undergoing open repair (39%) and nonenrolled (41%) patients, virtually all of whom underwent open repair (P value of 2% difference with 95% CI). This again corroborates comparability between the enrolled and nonenrolled groups. Thus, we believe that our conclusions, which were based on the patients enrolled, may still be generalizable to the larger population of rAAA patients.

Conclusions

Questions that were answered in the present study included that eEVAR appeared to be a feasible method for most dedicated vascular centers to treat rAAA. Also, a good outcome may be anticipated for most patients. The mortality after eEVAR was 35% and the overall mortality was 37%, which compared favourably with most previously published results of open repair.[3-7] In the simultaneously nonenrolled group, mortality was 41% after open repair. Half of the patients with rAAA in our study were treated by endovascular technique, which is higher than in most previous studies.
The availability and number of endovascular teams with experience in emergency endovascular repair needs to improve to include most patients with a ruptured infrarenal abdominal aneurysm in a preferential treatment by EVAR protocol. In a well-organised setting, the advantages of less blood loss, avoiding of laparotomy, and shorter time in the intensive care unit and on mechanical ventilation should translate into a further decrease of the perioperative mortality.

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Author contributions

Conception and design: NP, JB
Analysis and interpretation: NP, EB, JB
Data collection: NP, RHG, CS, PC, OKS, JAWT, ML,JDL, FEGV, GD
Writing the article: NP, JB
Critical revision of the article: EB, RHG, CS, PC, OKS,JAWT, ML, JDL, FEGV, GDR, JB, NP
Final approval of the article: EB, RHG, CS, PC, OKS,JAWT, ML, JDL, FEGV, GDR, JB, NP
Statistical analysis: NP, EB, JB
Obtained funding: JB
Overall responsibility: JB

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Appendix: Participants of the new ERA study

Participants
Medisch Spectrum Twente, Enschede, the Netherlands: R.H. Geelkerken, A.B. Huisman, D.J. Gerrits, E.D.P. Volker, R. van Det, P. de Smit (23);
Regional Endovascular Centre, Belfast, Northern Ireland: C. Soong, C. Boyd, W. Loan (18);
Catharina Hospital, Eindhoven, the Netherlands: J. Buth, Ph. Cuypers, N. Peppelenbosch (14);
Policlinico Monteluce, Perugia, Italy: P. Cao, F. Verzini, S. Mosca (11);
Royal Victoria Hospital, Montreal, Quebec, Canada: O.K. Steinmetz, K. MacKenzie, D. Obrand, B. Montreuil (11);
Atrium Medisch Spectrum, Heerlen, The Netherlands: J. Teijink, H. Odink, R. Welten (8);
Meilahti Hospital/HUCH, Helsinki, Finland: M. Lepäntalo, P. Keto, W. Roth, P. Aho (5);
AZ St. Jan AV, Brugge, Belgium: J. de Letter (5); University Hospital, Gent, Belgium: F.E.G. Vermassen, Ivan Herzeele (3);
London Health Sciences Centre, London, Ontario, Canada: G. DeRose, T.L. Forbes, S.W. Kribs (2).

Adverse Event Advisory Committee
B. Barbieri, Medtronic, Maastricht, the Netherlands;
J. van den Berg, Lugano, Italy;
P. Cao, Policlinico Monteluce, Perugia, Italy;
S. Zannetti, Medtronic, Santa Rosa, Calif.

Steering Committee
B. Barbieri, Medtronic, Maastricht;
J. Buth, Ph. Cuypers, and J. Jakimowicz, Catharina Hospital, Eindhoven, The Netherlands; and
S. Zannetti, Medtronic, Santa Rosa, Calif.

CHAPTER VIII

General discussion and conclusions

General discussion

In spite of the improvements in anaesthetic techniques and intensive care methods the mortality rate of ruptured abdominal aortic aneurysms has remained high since first treatments were reported in the mid-fifties of the previous century. A recent meta-analysis by Bown and colleagues demonstrated a modest decline in mortality of open repair of patients with ruptured AAA during the past three decades. The mean mortality rate was calculated at 41% in the year 2000.[1] However, several recent reports demonstrated higher mortality rates, ranging from 46 to 54%.[2-5] The operative technique has remained largely unchanged over the years. The possibility that endovascular treatment might further reduce the mortality rate was examined in this thesis.

In the late twentieth century a novel operating technique was introduced for elective abdominal aortic aneurysms (AAA). Parodi and colleagues introduced in 1991 an endovascular technique for repair of elective abdominal aortic aneurysms.[6] Reports published thereafter showed decreased post-operative mortality rates in elective AAA repair. In *Chapter II* we assessed whether the size of an abdominal aortic aneurysm (AAA) was of any influence on the results of elective AAA repair by endovascular technique. The outcome of this analysis was that size was an independent predictor for aneurysm-related death, all-cause death and rupture, i.e. the larger aneurysms were associated with a higher event risk. A subsequent conclusion involved that endovascular devices were associated with the best results in small aneurysms. The superior outcome of treatment in the small aneurysm category were due to less complex anatomy resulting in reduced rates of procedural complications and adverse events during follow-up compared to patients with large aneurysms. In addition, patients in the small aneurysm category were in better medical condition. The latter finding suggests that size is related to the patient's general medical condition. These observations indicate that in future studies the outcome of patients treated with endovascular devices must be stratified according to the size of their aneurysms.

As the balance between risk and benefit of intervention in patients with small aneurysms (4.1 - 5.4 cm) may be more favourable with endovascular treatment a potential implication may be that the accepted threshold for treatment of AAA, now 5.5 cm for open repair, may be lower in patients receiving endovascular repair (EVAR). The possible benefit of EVAR in small aneurysms is currently subject of two interventional multicenter studies, the CAESAR-study in Europe and the PIVOT- study in the USA.[7] Of note is that the general condition and life expectancy in these patients also needs consideration as the annual risk of rupture of small aneurysms is substantially lower. In other words a risk-benefit analysis needs a longer horizon. A decision to treat a patient with a small abdominal aortic aneurysm by stentgrafting must also account for the risk of a late complication or the need for a reintervention. In all patients treated by endovascular technique there remains the need for a long-term surveillance by imaging technique.

In *Chapter III* we described the feasibility of emergency EVAR (eEVAR) in selected patients with rAAA. In relatively haemodynamically stable patients we and other

groups demonstrated that it was possible to perform an emergency CT examination and an emergency EVAR procedure successfully when the anatomical characteristics were favourable for endovascular repair. Stentgraft repair can be performed using local anaesthesia, which was our preferred technique, because then the insecure hemodynamic situation is not disturbed. The feasibility of eEVAR in a proportion of patients with ruptured AAA and favourable conditions was now established. These initial reports described the outcome of eEVAR in patients selected on the basis of availability of staff and haemodynamic stability. Although the outcome in this group was excellent it is unknown what the result would have been with an open procedure and further analysis is required.

In *Chapter IV* we reported the outcome of eEVAR in a prospective study of a cohort of patients treated on an intent-to-treat by eEVAR protocol. This protocol described the treatment at the emergency department on arrival in the hospital, the transportation to the radiology department when this was possible considering the additional time involved, and the procedure of eEVAR in the operating theatre. Main features in this protocol were lowering intravenous fluid infusion rate when possible at arrival in the hospital, emergency CT examination and quick transportation hereafter to the operating theatre. When endovascular repair was possible local anaesthesia was preferred and an aorto-uni-iliac endograft system in combination with a femoro-femoral crossover bypass was used.

In *Chapter IV* the series differed from those in Chapter III since all comers with ruptured AAA were enrolled into the series and treated according to the described protocol. A suitable anatomy constituted the main criterion to qualify for emergency endovascular repair. The conclusion of this report was that eEVAR was technically and logistically feasible in the majority of unselected patients with an acute AAA. The applicability rate of eEVAR in the current series (62%) was substantially higher than reported in series from other institutions. A possible explanation for this high rate may be the use of less restrictive inclusion criteria regarding the aneurysmal neck (shorter necks accepted), the use of aorto-uni-iliac (AUI) stentgrafts with a known wider application in comparison to aorto-bi-iliac stentgrafts. With the use of AUI stentgrafting patients with one iliac artery unsuitable for access still qualify for stentgraft treatment. The recruitment of patients with more severe hemodynamic instability as candidates for eEVAR may also have increased our use of the stentgraft technique.

The observations described in *Chapter IV* included significant less blood loss and a diminished need for intravenous fluid in the perioperative period in patients with eEVAR. As for the main outcome event, the in-hospital or 30-day mortality rate in the overall study group of patients with rAAA, e.g. patients treated with eEVAR and open repair combined, was 31%. This mortality rate was substantially lower than the approximately 50% mortality rate reported in most series on treatment by open repair. This was the first published report that compared a cohort of patients with rAAA treated with preferential eEVAR, i.e. endovascular repair when possible, and made a comparison of the overall series (eEVAR and open repair combined) with a historical control group. Although the reported morbidity rate in most publications on eEVAR is less in compar-

ison with open repair, many complications were not accurately assessed. Among these adverse events post-operative spinal cord ischaemia was not studied in detail and the occurrence is perhaps under-reported after treatment of patients with rAAA.

Chapter V describes a relatively high rate of spinal cord ischaemia of 11.5% in a combined series of the Catharina Hospital, Eindhoven, Onze Lieve Vrouwe Gasthuis, Amsterdam and University Hospital, Gent. All patients were treated by an aorto-uni-iliac stentgraft in combination with a femoro-femoral crossover bypass. The aetiology of spinal cord ischaemia is probably multifactorial. However, from the analysis that we performed it became apparent that occlusion of a hypogastric artery correlated statistically significant with spinal cord ischaemia. In addition the time window in which one or two hypogastric arteries were not perfused during the procedure, appeared also significantly associated with the occurrence of paraplegia. Patients at risk for this complication are those who have common iliac artery aneurysm requiring interruption of hypogastric arterial inflow. Spinal cord ischaemia, once it had occurred, was associated with a statistically higher risk of post-operative death. The recording of only death as a main complication may be an explanation why spinal cord ischaemia is probably under-reported in series on open repair.

The feasibility of endovascular repair was established in *Chapter III* and the cohort report described in *Chapter IV* suggested better outcome after endovascular repair in rAAA patients. At this point a larger multicenter series was needed to assess the applicability rate, e.g. in how many patients with rAAA is endovascular repair possible. Emergency EVAR would not have much impact if only a small minority of patients with rAAA can be treated by eEVAR. Other pertaining questions are the following: what are the main exclusion criteria for eEVAR? What logistical problems can be encountered when an eEVAR program is introduced in an institution? The most important question involves whether there is indeed a better outcome from eEVAR? A prospective multicenter international trial, organised and sponsored by Medtronic-AVE, indicated as the "New ERA" study (Endograft treatment of Ruptured abdominal aortic Aneurysm) was scientifically conducted by the Vascular Surgical Unit from the Catharina Hospital in Eindhoven, the Netherlands. A detailed protocol describing study design, inclusion criteria, diagnostic algorithm and treatment steps was outlined. This study included a cohort of one-hundred patients treated for rAAA following a policy of preferential treatment by eEVAR. The protocol and study design of the New ERA study are presented in *Chapter VI*. The diagnostic algorithm determined on the basis of the triage of patients at the emergency department. CT examination of all patients except those with severe haemodynamic instability or severe cardiac arrhythmias. Important other features in this study included the exclusive use of the Talent® Aorto-uni-iliac device, preventing the use of more than one brand of device. A variety of stentgrafts may obscure the interpretation of data. Permissive hypotension was adhered to, to limit retro or intraperitoneal blood loss. The study protocol required a permanent availability of an endovascular experienced specialist team.

Chapter VII reported the outcome of this multicenter study. Of one-hundred patients treated for rAAA 49 received endovascular repair and 51 open repair. The primary rea-

son to perform open aneurysm repair was an unfavourable configuration of the neck in 80% of the patients. In patients receiving eEVAR operative blood loss was less, duration of mechanical ventilation and intensive care admission time were shorter (p = 0.02, all comparisons). The primary outcome event was the 30-day or in-hospital mortality in the overall series, which was 37%. This is substantially lower than the mortality rates in patients with open repair, which varies in the recent literature from 46 to 53%. It is emphasised that this assessment is the first in literature of unselected cohorts of patients presenting with rAAA.

The outcomes in the two subgroups, with endovascular (35% mortality) and open repair (39% mortality), is also interesting. The mortality in the endovascular treated patients was lower than in the open repair subgroup, although this difference was not significant. The mortality rate of the group with open repair was relatively low. A likely explanation may be that a number of poor risk patients with suitable anatomy were now treated by endovascular technique. In this pragmatic study, "endovascular treatment for each patient unless…" was the guideline. This mechanism not only may have caused an overall improved first-month mortality (compared to the usual 50% mortality in open repair series), but also may have a favourable effect in the open repair subgroup because some high-risk patients shifted to endovascular repair.

The hospitals that participated in the study all had a documented experience in endovascular and open repair in patients with rAAA. Nevertheless, the New ERA study demonstrated a number of unexpected flaws including a high exclusion rate of patients because of unavailable endovascular specialists during on rota calls. However, when analysed closely, the high number of exclusions can be considered a random effect and it was considered not to influence the mortality rates in the entire group or the subgroups. The following conclusions may be drawn from the New ERA study: (1) stent-graft treatment is feasible in approximately 50% of patients presenting with rAAA; (2) eEVAR probably has a favourable impact on the first-month survival of the entire cohort with rAAA; (3) further clinical studies are needed to confirm these outcomes. The high rate of unavailable endovascular specialists in this series is worrisome since the recruited hospitals were selected hospitals with acknowledged experience in the endovascular field. Shortage of endovascular specialists must be addressed by intensifying training in this area. Senior surgical trainees with an interest in a vascular career and specialists in training as vascular surgeon should acquire these techniques and obtain a substantial practical experience.

It is important to make clear that the most important outcome in patients with rAAA is in-hospital or 30-day survival. This primary outcome event differs from patients with elective repair, in whom long-term survival, re-intervention rates and freedom of rupture are considered equally important. After patients with rAAA have survived operation they can be managed at the intensive care unit for securing a stable haemodynamic condition, supporting oxygenation, preventing kidney failure and treatment or prevention of other complications. If necessary secondary procedures can be performed after stabilization of the patient. In case type I and/or type III endoleaks are present and cannot be controlled at the initial procedure, the patient is first stabilised

in the intensive care unit and a secondary endovascular or open procedure may be performed at a later time to deal with this problem, similar as in patients with elective EVAR.

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CHAPTER IX

Samenvatting

Aneurysma van de aorta abdominalis

Een aneurysma is een permanente, lokale verwijding van een slagader met een 50% of grotere diameter in vergelijking met de verwachte normale diameter.[1] Hoewel aneurysmata in het gehele traject van de aorta kunnen ontstaan is de abdominale aorta een voorkeurslokalisatie. Hier wordt het aneurysma in 75% aangetroffen.[2] Het vóórkomen van een aneurysma aortae abdominalis (AAA) in Nederland wordt bij mannen ouder dan 55 jaar geschat op 4,1% en bij vrouwen op 0,7%.[3] Risicofactoren om een AAA te ontwikkelen zijn oudere leeftijd, mannelijk geslacht, roken, een positieve familie anamnese voor aneurysmata, arteriosclerose en hoge bloeddruk.[4,5]

Risicofactoren voor ruptuur

Een aneurysma van de aorta abdominalis geeft in het algemeen geen klachten tot een ruptuur optreedt. Het typische klachtenpatroon van een geruptureerd aneurysma bestaat uit acute pijn in de buik, eventueel gepaard gaande met rugpijn, met signalen van haemodynamische shock zoals collaps, een lage bloeddruk en een snelle pols. Indien er geen operatie wordt uitgevoerd is de gemiddelde tijd tussen het arriveren in het ziekenhuis tot overlijden 7 à 10 uur. De maximale tijd van overleving in een tweetal gepubliceerde series was 6 dagen.[6,7] Bij operatie wordt het aneurysma vervangen door een kunststof prothese. Gerbode beschreef in 1954 deze operatie voor het eerst bij een patiënt met een geruptureerd aneurysma.[8] In de loop van de tijd zijn aanpassingen ingevoerd, echter de principes zijn hetzelfde gebleven. Via een mediane laparotomie wordt de proximale aorta vrij gelegd om een vaatklem te kunnen plaatsen. Na afklemming wordt het aneurysma geopend en worden bloedende lumbale arteriën doorstoken. Nu wordt een kunststof buis of bifurcatieprothese geplaatst en de anastomoses geconstrueerd middels de zogenaamde inlay techniek. Vervolgens wordt de vaatklem afgenomen en de bloedstroom naar beide benen weer vrijgegeven. De kunststof buis- of bifurcatieprothese wordt vervolgens bedekt door de aneurysma wand weer naar elkaar toe te hechten. Ondanks de verbeteringen op het gebied van de anaesthesie en de intensive care geneeskunde kent deze operatie, indien het aneurysma gebarsten is, een slechte prognose. Het risico op overlijden in de fase direct na de operatie (de 30-dagen- of ziekenhuismortaliteit) werd geschat op 41% in het jaar 2000.[9] Dit percentage was berekend door middel van een meta-analyse. Echter een aantal studies van recentere datum vermelden weer een beduidend hogere postoperatieve mortaliteit, variërend van 46 tot 54%.[10-13]

In twee gerandomiseerde studies, waarin de ruptuurkans van intacte aneurysmata werd onderzocht, werd aangetoond dat de kans op ruptuur laag is bij een diameter kleiner dan 5,5 cm.[14,15] In deze studies werd de kans op ruptuur bij een diameter tussen de 4,0 en 5,5 cm geschat tussen de 0,6 en 1%. Dit is inderdaad een veel lagere kans dan bij patiënten met een diameter tussen de 5,5 en 6,0 cm die geen operatie ondergingen. Deze patiënten waren in een te slechte conditie voor een ingreep of

wilden geen operatie ondergaan. Bij deze patiënten was de kans op een ruptuur 9,4% in het eerste jaar.[16] Een AAA wordt in principe behandeld indien de kans op overlijden door een ruptuur groter is dan de kans op overlijden door een electieve operatie. Met bovenstaande waarden als referentie komt men dan op een diameter van het AAA ≥ 5,5 cm als grenswaarde voor een operatie.

Endovasculaire behandeling van het aneurysma aorta abdominalis

In het begin jaren '90 van de vorige eeuw werd de endovasculaire techniek geïntroduceerd door Parodi en medewerkers voor de electieve behandeling van het AAA.[17] Het betrof een methode waarbij een kunststof prothese gewapend met een metalen draadwerk (daarom een stentgraft genoemd), in gecomprimeerde vorm via de liesslagader wordt ingebracht en opgevoerd tot net onder de nierslagaders. In die positie wordt de stentgraft ontplooid, waarbij het aneurysma van de systemische bloedstroom wordt afgescheiden. Het stentdeel bestaat uit "geheugenmetaal" en neemt zijn oorspronkelijke vorm aan (ontplooit) nadat de inbrenghuls is teruggetrokken. Door het opblazen van een ballon in de stentgraft wordt de endograft verder geëxpandeerd, zodat deze stevig tegen de aorta wand wordt aangedrukt. Publicaties die volgden over deze methode, genaamd EVAR (endovascular abdominal aortic aneurysm repair), lieten een vermindering zien van de postoperatieve sterfte in vergelijking met de open procedure. De ingreep werd gedurende vele jaren uitsluitend bij de behandeling van niet-geruptureerde aneurysmata toegepast.

In *Hoofdstuk II* bestudeerden we of de diameter van het aneurysma van invloed is op de uitkomst van de electieve EVAR-behandeling. We constateerden dat na plaatsing van een endograft de diameter van een aneurysma een onafhankelijke voorspellende variabele is voor: (1) aneurysma-gerelateerde dood, (2) niet-aneurysma-gerelateerde dood en (3) kans op ruptuur nadat een endograft is geplaatst. Met andere woorden, een endograft geeft de beste resultaten bij een klein aneurysma. De waarschijnlijke verklaring hiervoor is dat kleine aneurysmata een minder complexe anatomie hebben, waardoor minder procedure-gerelateerde complicaties optreden en minder complicaties tijdens follow-up ontstaan. We constateerden ook dat des te groter de diameter van het aneurysma hoe slechter de medische toestand van de patiënt is. De diameter houdt dus verband met de algehele medische toestand van de patiënt. Het is dan ook raadzaam om in toekomstige studies de uitkomst na EVAR te relateren aan de diameters van de behandelde aneurysmata. Uit onze observaties zou men tevens kunnen concluderen dat de grens voor de behandeling van een AAA, nu 5,5 cm bij open procedures, mogelijk kan worden verlaagd bij EVAR-behandeling van aneurysmata. Dit laatste wordt nu onderzocht in een Europese en een Amerikaanse studie, namelijk de CAESAR en de PIVOT trial.[18] Belangrijk is op te merken dat, hoewel stentgrafts betere resultaten geven bij kleinere aneurysmata, de kans op ruptuur in deze patiëntengroep ook kleiner is. Derhalve dienen steeds de met EVAR, gepaard gaande complicaties, secundaire interventies en de noodzaak van levens-

lange follow-up, afgewogen te worden tegen het voordeel van preventie van ruptuur van het aneurysma.

In *Hoofdstuk III* werd onderzocht of het mogelijk is om een endovasculaire procedure te verrichten bij patiënten met een geruptureerd aneurysma. Patiënten met een gesprongen AAA presenteren zich op onvoorspelbare tijdstippen tijdens de diensturen in het ziekenhuis. Het was daarom van belang de ingreep, die dientengevolge veelal met in endovasculair opzicht ongeoefend medische en paramedische assistentie moet worden uitgevoerd, verregaand te vereenvoudigen. De vaatchirurgie van het Catharina ziekenhuis te Eindhoven greep hiervoor terug op een oorspronkelijke techniek, de aorto-uni-iliacale stentgraft met endovaculaire occlusie van de contralaterale iliaca en een crossover femoro-femorale bypass. Het concept werd zodanig gemodificeerd dat het geschikt werd voor de spoedbehandeling van het acute AAA. De firma Medtronic-AVE was bereid de aangepaste versie te produceren en heeft het op de markt gebracht als "Emergency AAA kit". Voor dit deel van onze studie werden patiënten geselecteerd welke haemodynamisch stabiel waren. We konden aantonen dat bij deze geselecteerde patiënten het mogelijk was om met spoed een CT-scan te verrichten, deze terstond te beoordelen op geschiktheid van de anatomie voor een endoprothese om vervolgens een urgente EVAR- procedure uit te voeren. Ook toonden we aan dat de acute procedure onder lokale of regionale anesthesie uitgevoerd kon worden. Het bleek dat de resultaten in deze geselecteerde groep bevredigend waren, met een 1e-maands mortaliteit van 24%. De meeste publicaties van andere groepen noemden een mortaliteitspercentage van 10%.[19-23] Na deze studie bleef nog onzeker hoe de resultaten van de endoprocedure zich verhouden met die van conventionele chirurgische behandeling. Immers, bij vergelijkbaar haemodynamisch stabiele patiënten met gunstige anatomische karakteristieken kan men van conventionele chirurgie eveneens redelijk goede resultaten verwachten. Ook moest nog nagegaan welk percentage van de patiënten met een geruptureerd aneurysma voor acute EVAR in aanmerking kwam.

In *Hoofdstuk IV* werd een ander cohort van patiënten met een geruptureerd AAA onderzocht. In dit deelonderzoek werden patiënten geïncludeerd bij wie "zo mogelijk" een endovasculaire procedure werd uitgevoerd, dit wil zeggen bij aanwezigheid van geschikte anatomische kenmerken en acceptabele haemodynamische conditie ("intention-to-treat by EVAR" of "preferential endovascular repair"). Indien een endovasculaire procedure niet kon worden uitgevoerd werd een conventionele open ingreep uitgevoerd. Hiertoe werd een protocol opgesteld waarin de behandeling van de patiënten op de spoedeisende hulp, het transport naar de afdeling radiologie voor het vervaardigen van een CT-scan en de operatieprocedure werd beschreven.

Na aankomst op de spoedeisende hulp afdeling werd de patiënt aangesloten op een monitor voor haemodynamische bewaking. Vochttoediening via infusen werd geminimaliseerd en hypotensie werd tot zekere hoogte geaccepteerd ("permissive hypotension"). Indien er geen ernstige hartritme stoornissen aanwezig waren en de bloeddruk acceptabel was (> 60 mmHg) werd de patiënt getransporteerd naar de radiologie afdeling voor een spoed CT-scan. Ruptuur van het aneurysma werd

gedefinieerd als bloed buiten de wand van het aneurysma. De lengte en de diameter van de hals werden gemeten en beoordeeld werd of het aneurysma geschikt was voor endovasculaire behandeling. De uitkomst werd doorgegeven aan de anesthesist en de staf van de operatieafdeling. Hierna werd de patiënt snel getransporteerd naar de operatiekamer.

Indien een endovasculaire procedure kon worden uitgevoerd werd primair voor lokale anesthesie gekozen. Een van beide liezen werd geïnfiltreerd met lidocaine en de arteria femoralis werd vrij geprepareerd. Een voerdraad en een angiografie katheter werden achtereenvolgens via deze arterie opgevoerd. De nierslagaders werden afgebeeld en gemarkeerd op de röntgenmonitor. Vervolgens werd de hoofdcomponent van de stentgraft opgevoerd en ontplooid. Hierna werd een iliacale verlenging geplaatst waarbij het distale stentgraftdeel in de arteria iliaca communis diende te landen. De gebruikte modificatie van de aorto-uni-iliacale stentgraft (zie hierboven), werd ingebracht via de ipsilaterale liesarterie. Indien mogelijk werd voor het vervolg van de procedure de andere lies met lokale anaesthetica geïnfiltreerd. Echter als de patiënt te onrustig of teveel pijn ondervond, werd op algehele anesthesie overgegaan voor de verdere operatie. De contralaterale arteria iliaca werd vervolgens afgesloten met een ingebrachte zogenaamde "occluder" stentgraft, om te voorkomen dat retrograad het aneurysma aan systemische bloeddruk blootgesteld bleef. Hierna werd een femorofemorale cross-over bypass aangelegd om het contralaterale been van bloed te voorzien. Een controle angiografie werd verricht om endolekkage (vulling van het aneurysma vanuit de systemische circulatie) aan te tonen of uit te sluiten. Type II endoleaks werden geaccepteerd, type I en III endoleaks dienden in dezelfde procedure te worden gecorrigeerd.

In de klinische studie die in *Hoofdstuk IV* wordt beschreven, werd elke patiënt met een symptomatisch aneurysma (zowel geruptureerde als niet geruptureerde aneurysma's) opgenomen. Volgens bovenstaand protocol werden de patiënten bij voorkeur behandeld met een endovasculaire behandeling, d.w.z. indien mogelijk op grond van de aorto-iliacale anatomie en de haemodynamische toestand. Patiënten werden met een open procedure behandeld indien zij haemodynamisch te instabiel waren om een CT-scan te ondergaan. Van deze categorie konden daarom geen anatomische gegevens verkregen worden en geschiktheid voor endovasculaire behandeling kon niet worden bepaald. Niettemin kon uit dit onderzoek worden geconcludeerd dat een meerderheid van de patiënten op grond van geschikte anatomie wèl endovasculair behandeld kon worden (n.l. 62%) Dit percentage verschilde beduidend van de ervaring in publicaties uit andere centra, waar tussen de 27 en 37% van de patiënten met een stentgraft kon worden behandeld.[20,21,23] Verschillende redenen kunnen worden aangevoerd om dit verschil te verklaren. Ten eerste werden onze patiënten behandeld met een aorto-uni-iliacale (AUI) prothese i.p.v. een bi-iliacale prothese, waardoor slechts één iliacale vaat-as geschikt hoeft te zijn als toegang voor het plaatsen van een prothese. Ten tweede, endografts van sommige firma's worden niet in grotere diameters geleverd, waardoor bij patiënten met een geruptureerd aneurysma, waarin juist deze implantaten frequent zijn aangewezen, minder vaak voor eEVAR kan wor-

den gekozen. Ten derde werden minder strikte anatomische criteria in de situatie van een geruptureerd AAA aangehouden dan in een electieve situatie gebruikelijk is. Met name werd een kortere infrarenale nek vaker geaccepteerd. Dit was in versterkte mate het geval bij patiënten welke geacht werden een slechte kans te hebben op overleven indien een open procedure werd uitgevoerd.

De verdere observaties van dit onderzoek betroffen: significant minder bloedverlies en een geringere behoefte aan intraveneuze vloeistoffen bij acute EVAR-patiënten. De belangrijkste bevinding was een lagere 30-dagen mortaliteit. Deze was voor de gehele groep (zowel endovasculair als open geopereerde patiënten met een geruptureerd aneurysma) 31%. Dit was beduidend lager dan de in de literatuur genoemde mortaliteitspercentages na conventioneel chirurgische behandeling, welke varieert van 46% tot 54%.[10-13] Onze studie betrof de eerste publicatie, waarin een totaal cohort van patiënten met een "in principe endovasculaire behandeling" op deze wijze werd vergeleken met open behandeling in een historische controlegroep uit de literatuur.

Hoewel de belangrijkste uitkomstmaat overleving in de gehele studiegroep is, bleek uit de in *Hoofdstuk IV* beschreven studie, na subgroep analyse, dat ook de morbiditeit lager was na een endovasculaire behandeling. Een aantal vormen van postoperatieve morbiditeit na endograft behandeling voor rAAA dienden nog nader onderzocht te worden. Eén van deze complicaties betrof postoperatief ontstane ruggenmerg-ischemie, een complicatie die vrij zeldzaam geacht wordt voor te komen.

Hoofdstuk V beschrijft een gecombineerde serie van patiënten met deze aandoening uit drie ziekenhuizen, het Catharina-ziekenhuis te Eindhoven, het Onze Lieve Vrouwe Gasthuis te Amsterdam en het Universiteitsziekenhuis te Gent. Bij patiënten met een geruptureerd AAA die behandeld werden met een AUI stentgraft werd in deze gecombineerde serie een relatief hoge prevalentie van ruggenmerg-ischemie waargenomen, n.l. 11,5%. Hoewel de oorzaak van spinale ischemie multifactorieel van aard is, bleek dat de arterie iliaca interna (arteria hypogastrica) statistisch significant vaker moest worden geoccludeerd tijdens de procedure bij patiënten met ruggenmerg-ischemie. Ook was de tijdsduur van de tijdelijke afsluiting van de arterie iliaca interna tijdens het inbrengen van de endograft significant langer vergeleken met patiënten die postoperatief geen ruggenmerg-ischemie ontwikkelden. Patiënten met postoperatieve ruggenmerg-ischemie hadden verder een statistisch significant grotere kans op overlijden. Dit kan suggereren dat er een onderrapportage van paraplegie zou kunnen bestaan in eerdere publicaties betreffende de geruptureerde AAA's. Mogelijk wordt van deze patiënten alleen mortaliteit als complicatie geregistreerd.

De cohortstudie uit *Hoofdstuk IV* toonde een lagere postoperatieve mortaliteit, in een patiëntencohort met acute AAA's in vergelijking tot de 1e-maands mortaliteit in series met uitsluitend open chirurgie, zoals vermeld in de literatuur. Niet beslissend was aangetoond dat deze verbetering het gevolg was van de endovasculaire behandeling van een deel van het studiecohort Een grotere multicentrische prospectieve studie zou deze vraagstelling kunnen beantwoorden. Voorts zou zo'n studie beter inzicht kunnen geven over het percentage patiënten met een anatomisch en heamodynamisch voldoende goede toestand om in aanmerking te komen voor deze behan-

deling. De endovasculaire behandeling zou immers minder impact hebben indien slechts een minderheid van diegenen met een rAAA hiervoor in aanmerking zou komen. Ook kan een multicenterstudie helpen exclusiecriteria te formuleren voor een spoed-EVAR.

Welke logistieke problemen kunnen worden verwacht? Bedacht moet worden dat de klassieke "open" ingreep al meer dan 40 jaar de routineprocedure vormt en daardoor in ziekenhuizen sterk is ingeburgerd. De belangrijkste vraag blijft of de postoperatieve mortaliteit van rAAA in het algemeen daadwerkelijk wordt verminderd door het toepassen van een endovasculaire behandeling. Het team in het Catharina-ziekenhuis kreeg de kans een prospectieve internationale multicentrische trial, ondersteund en gefinancierd door Medtronic-AVE, te organiseren. Deze studie werd genoemd de "New ERA study" (Endograft treatment of Ruptured abdominal aortic Aneurysm). De opzet, het protocol en studieontwerp voor de New ERA studie werden beschreven in *Hoofdstuk VI*. De diverse factoren welke de resultaten van behandeling van een rAAA kunnen beïnvloeden dienden in dit onderzoek te worden geanalyseerd. Honderd patiënten die werden behandeld voor een geruptureerd aneurysma met als voorkeursbehandeling de endovasculaire techniek vormden de studiegroep. Belangrijk was ook dat de onderzoeksgroep werd gevormd door patiënten die een stentgraft ofwel een open behandeling ondergingen. De twee afzonderlijke behandelingscategorieën werden als "subgroepen" aangeduid. Alleen patiënten met een met zekerheid aangetoonde ruptuur van het aneurysma werden geïncludeerd. De belangrijkste elementen van het protocol zijn verder het gebruik van eenzelfde type stentgraft, de Talent® AUI stentgraft en een nauwkeurige beoordeling van de haemodynamische conditie van patiënten op de spoedeisende hulp afdeling. Een CT-scan werd gemaakt bij alle patiënten met uitzondering van haemodynamisch ernstig instabiele patiënten. Zij ondergingen zo mogelijk fluoroscopische afbeelding van het aneurysma op de operatiekamer. Op grond van het beeldvormend onderzoek werd gekozen voor endograft of open chirurgische behandeling. Het studieprotocol vereiste een permanente 24-uurs bezetting van een ervaren endovasculair team.

Hoofdstuk VII rapporteert over de uitkomsten van deze multicentrische studie. Van de 100 behandelde patiënten ondergingen 49 patiënten een endovasculaire procedure en 51 een open procedure. De belangrijkste reden voor een open procedure was een ongeschikte anatomie van de infrarenale hals. Dit was het geval in 80% van de patiënten met een open procedure. Indien een endovasculaire procedure werd uitgevoerd was er minder bloedverlies, een kortere intensive care opname en een kortere beademingstijd. Alle verschillen waren statistisch significant ($p < 0.02$). De 30-dagen mortaliteit in de totale onderzoeksgroep was 37%, in de endovasculair behandelde subgroep 35% en in de subgroep met een open procedure 39%. Het verschil tussen de beide subgroepen is niet significant. Het belangrijkste mortaliteitscijfer is dat van de gehele onderzoeksgroep. Dit percentage is beduidend lager dan de ongeveer 50%, welke gewoonlijk wordt waargenomen in series met open chirurgie. Verder valt op dat de mortaliteit in de subgroep met open chirurgie in de New ERA-study lager is dan gebruikelijk voor deze operatie. Een mogelijke verklaring hiervoor is dat een aan-

tal patiënten met een aanzienlijk verhoogd operatierisico doch een gunstige anatomie geselecteerd werden voor een endovasculaire behandeling. Immers, in deze pragmatische studie gold "endovasculaire operatie voor iedere patiënt tenzij…". Dit principe kan tot gevolg hebben dat niet alleen het mortaliteitspercentage in de totale groep daalt, maar ook in de subgroep met open behandeling (door verschuiving van hoogrisico patiënten naar de endograftcategorie). Dit effect, hoewel aannemelijk, is niet met zekerheid aangetoond. De conclusies van de studie kunnen als volgt worden samengevat: (1) stentgraftbehandeling is een geschikte behandeling bij ongeveer 50% van de patiënten met rAAA; (2) eEVAR heeft mogelijk een gunstig effect op de 1e-maands overleving van een totale patiëntengroep met rAAA; (3) meer klinische studies zijn aangewezen om deze resultaten te bevestigen.

De ziekenhuizen die participeerden in de studie hadden een ruime ervaring met geruptureerde aneurysmata zowel met de open procedure als met de endovasculaire procedure. Deze New ERA-studie had niettemin een aantal onverwachte tekortkomingen van logistieke aard. Ten eerste was een groot aantal patiënten geëxcludeerd van de studie door het niet beschikbaar zijn van endovasculaire specialisten. Nadere analyse toonde dat het excluderen van deze patiënten overigens geen invloed had op de uitkomsten van de New ERA studie. Het frequent niet aanwezig zijn van een endovasculair specialistisch team is evenwel zorgwekkend. Het tekort aan endovasculair gespecialiseerde teams vraagt om een beter gestructureerde intensieve scholing op dit gebied. Ouderejaars chirurgische assistenten met carrièreplannen voor vaatchirurgie en specialisten in opleiding tot vaatchirurg dienen met de EVAR-techniek niet alleen vertrouwd te zijn maar ook een substantiële praktische ervaring te hebben opgebouwd. Indien gespecialiseerde ziekenhuizen geen 24-uurs bezetting kunnen realiseren, heeft dit tot gevolg dat de endovasculaire techniek niet doorlopend beschikbaar is.

Spoed-EVAR is een nieuwe behandelingsmethode die bij een groot deel van de patiënten met een geruptureerd aneurysma kan worden toegepast. Het is waarschijnlijk, maar niet onomstotelijk aangetoond, dat een overlevingsvoordeel is te behalen. Een aantal zaken werden aangetoond in dit proefschrift. Er is minder bloedverlies, minder vocht hoeft te worden toegediend tijdens en na de operatie en de opnameduur op de intensive care is verkort evenals de tijd aan de beademingsapparatuur. De gepresenteerde onderzoeken tonen een overlevingsvoordeel aan voor de gehele groep (spoed EVAR behandelde patiënten en patiënten met een open of EVAR procedure gecombineerd) t.o.v. eerder gepubliceerde controlegroepen, waarin uitsluitend conventionele chirurgie werd toegepast. Het is belangrijk te realiseren dat de voornaamste uitkomstmaat voor patiënten met een geruptureerd aneurysma de korte termijn overleving is. Ter vergelijking, bij patiënten met een electieve AAA-behandeling worden aan de overleving op de lange termijn, het percentage re-interventies en kans op ruptuur met een stentgraft in situ een even groot gewicht wordt toegekend als aan de vroege uitkomsten. Pas nadat patiënten met een geruptureerd aneurysma de operatie en de postoperatieve periode hebben doorstaan, worden de voornoemde eindpunten, zoals bij electieve ingrepen ook voor de acute groep relevant. Indien er endolekkage

van het type I en/of III aanwezig blijken dient de patiënt evenals na een electieve ingreep relatief spoedig een aanvullende endovasculaire of open procedure te ondergaan om de afwijking te verhelpen.

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CURRICULUM VITAE

Noud Peppelenbosch was born on January 6th 1969 in Oss, The Netherlands. He attended secondary school in Oss from 1981 until 1989 (MAVO St Jan, HAVO and VWO Titus Brandsmalyceum).

In 1990 he started his medical study at the Catholic University of Nijmegen, The Netherlands. Medical degree was obtained in May 1997 (Cum Laude). After two years working as a surgical resident at the department of Cardio-Thoracic surgery at the University hospital Nijmegen, he started working in 2000 as a surgical resident at the department of Surgery at the University hospital Maastricht. His surgical training started in 2001 at the Catharina hospital Eindhoven (dr. J.J. Jakimowicz) and from 2005 until 2007 he continued his training at the University hospital Maastricht (Prof.dr. J.W.M. Greve). He will start his vascular training in September 2007 (dr. G.W.H Schurink).

Noud Peppelenbosch is married to Esther Boots and they have two children, Luuk (November 2003) and Tim (April 2006).